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ALLERGY AND IMMUNITY IN OCULAR TUBERCULOSIS

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There is probably no subject in the whole domain of ophthalmology in regard to which more profound divergences of opinion between those best qualified to judge may be found than in regard to the efficacy and proper mode of administration of tuberculin in the treatment of ocular inflammation presumably due to tuberculosis. There are many who look on the drug as useless or dangerous. Among those who use the injections with the greatest enthusiasm, the poor results of their colleagues are explained as due to an improper mode of administration. However, one finds among those who advocate the use of tuberculin some who advise its intracutaneous administration, some who recommend subcutaneous injection and others who recommend intramuscular injection. Again one finds that the injections should be given every two weeks, twice a week, every other day; that they should be given in doses insufficient to produce a perifocal reaction, or that they should be given in doses just sufficient to produce a perifocal reaction. One gathers from such consideration that, in the absence of any rigid criteria for the diagnosis of many cases of ocular tuberculosis, many clinicians tend to regard those cases in which the patients do well on their pet method of inoculation as truly tuberculous, while those in which they do poorly may be attributed to some other type of infection.

In regard to the rationale of treatment with tuberculin, there is also a wide divergence of opinion, not only among ophthalmologists, but also among general clinicians and experimental pathologists. In the early days when Koch first prepared tuberculin, it was thought that active immunization would be achieved with this agent. It was soon found, however, that repeated inoculations of nontuberculous animals did not produce a reaction in these animals and did not protect them against subsequent infection with tubercle bacilli. On the other hand, tuberculous animals reacted violently to the injection of tuberculin, exhibiting local, perifocal and general reactions, depending on the dosage used—reactions now characterized as allergic.

From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital.

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It was found that animals once infected with tuberculosis become resistant to reinfection and allergic to tuberculin at about the same time, and the conception was gradually developed that allergy to the products of the tubercle bacillus was an aspect of immunity, and that the accelerated tubercle formation and increased inflammatory reaction about the tuberculous focus in allergic animals contributed to their general immunity to the infection. It was shown that the degrees of immunity and of allergy exhibit a rough parallelism, and that in measles, pregnancy, and miliary tuberculosis in which the resistance of the host seems to be impaired there may be a decrease in the allergy, as tested by intracutaneous injection of tuberculin. Based on this conception, a hypothesis as to the rationale of treatment with tuberculin has been formulated. If the allergic reaction normally present about the tuberculous focus is beneficial in healing the lesion, then an increase in this reaction should be more beneficial. It was, therefore, regarded as desirable to give the tuberculin in such dosage as to produce slight perifocal reactions. It was asserted that the perifocal reaction should be slight, for disastrous results were found in those cases in which severe perifocal reactions were obtained. Just why slight reactions should be beneficial when severe reactions were demonstrably bad has never been explained.

Recently, as the result of the work of Dr. Rich, a different conception of the relation of allergy to immunity in tuberculosis has grown up. It is not possible here to enumerate the great mass of evidence which Dr. Rich has brought together to support his thesis. In summary, it may be said that no essential difference has been discovered between allergy to tuberculin and allergy to other foreign proteins; that the death of young granulation tissue surrounding a tuberculous focus is directly caused by the allergy, and is of major importance in inducing the spread of the tuberculosis; that it has been possible in some experimental animals to bring about a temporary suppression of the allergic reaction without any concomitant loss of immunity, and that in a number of other infectious diseases a complete independence of allergy and immunity has been demonstrated. Dr. Rich concludes that the allergic reaction in tuberculous infection is a hindrance rather than a help to the immunity of the host.

On the basis of this, one would conclude that the aim of treatment with tuberculin should be the desensitization of the patient, rather than the production of slight perifocal allergic reactions, and such, indeed, is the procedure advocated by many of those who consider injections of tuberculin beneficial. It is interesting to note that in the treatment of pulmonary tuberculosis with tuberculin, which was pursued so strenuously twenty or more years ago, the occasional beneficial results were

found to occur in patients who lost their sensitivity to tuberculin in the course of their treatments.

The evidence supporting Dr. Rich's hypothesis is almost entirely indirect. Direct proof could be obtained only if an animal were made immune and allergic to tubercle bacilli, then completely desensitized to tuberculin, and then tested in order to discover whether the loss of allergy has been associated with an increase or a decrease in resistance to reinfection. This is the experiment, the results of which I am now reporting. The work has been carried on by Drs. Clarence Bernstein, H. Rothschild, H. F. Pierce and myself with the aid and advice of Dr. Rich.

The first step in this investigation was the attempt to discover whether or not desensitization to tuberculin could be achieved in tuberculous animals. For this purpose well nourished male guinea-pigs weighing from 450 to 500 Gm. were inoculated in the groin with a heavy suspension of tubercle bacilli of an avirulent strain known as R 1. This strain does not produce fatal, or even widespread, tuberculosis in animals so inoculated, the lesions being limited to the local lymph nodes with occasional solitary tubercles in the viscera. At the end of from three to four weeks, the guinea-pigs were found to have become allergic to tuberculin, as tested by intradermal inoculation of 5 mg. of old tuberculin. They were then given daily subcutaneous injections of old tuberculin, beginning with 5 mg., the amount being increased daily by 10 to 30 per cent until doses of from 1,500 to 2,000 mg. were reached. The size of these doses can be gaged by the fact that the equivalent dose in a man weighing 60 Kg. would be from 180 to 240 cc. of undiluted tuberculin. Animals obtaining these massive injections frequently developed sloughing sores in their skins, but did not, except after prolonged courses of injection, lose weight or exhibit other untoward symptoms. In fact, their condition on the whole was better than that of control animals who received equal injections of broth.

During the course of the inoculations, periodic tests of the allergic state by intradermal injections of tuberculin were given to the animals receiving tuberculin subcutaneously, and, also, to a similar group of control animals that had received the R 1 inoculation, but had had no subsequent treatment. The latter group, which I shall speak of as the "R 1 controls," maintained their allergy to tuberculin throughout the experiment; the group treated with tuberculin gradually lost their allergy until they were able to tolerate without reaction a dose of 100 mg. of undiluted old tuberculin injected intradermally. The loss of allergy was further tested by the Koch bacillus reaction, and also in some instances by the intraperitoneal injection of 2,000 mg. of old tuberculin. To the Koch bacillus reaction, which consists in the intradermal injection of living tubercle bacilli, the R 1 controls showed the typical positive reac-

tion consisting in accelerated tubercle formation and sloughing of the skin in from twenty-four to forty-eight hours. The animals treated with tuberculin showed for the most part no visible reaction to the injection. Normal control animals showed no immediate reaction, but developed tubercles and ulceration at the site of the inoculation in two weeks. R 1 controls given 2,000 mg. of tuberculin intraperitoneally died within six hours with signs of allergic shock. Normal controls and animals treated with tuberculin showed no reaction to the injection. From these tests, it is clear that practically complete desensitization of tuberculous guinea-pigs can be achieved. It must be noted that the dosage given these animals was incomparably greater than any now feasible in human beings, and the tuberculous guinea-pigs never achieve a degree of cutaneous allergy comparable to that found in human patients. Undoubtedly an attempt to desensitize human beings to an equivalent degree would be a herculean task, and one frought with the gravest danger.

In order to test the effect of desensitization on immunity, the desensitized guinea-pigs, the R 1 controls and a similar group of normal guinea-pigs were inoculated with virulent tubercle bacilli. It was thought desirable to test the immunity by three different criteria: (1) the mortality of the infection, (2) the degree of dissemination of the tuberculosis in the viscera and (3) the progress of the lesion at the site of inoculation. For the latter purpose, the eye seemed the ideal organ. Injections of virulent bacilli were, therefore, made in these three groups of guinea-pigs subcutaneously (to facilitate spread of the infection), intradermally (Koch test) and into the anterior chamber of one eye. The intra-ocular injections were made under ether anesthesia with a no. 28 gage needle thrust through the limbus and attached to a microinjection syringe, with which 0.005 cc. of a suspension of tubercle bacilli in salt solution was introduced into the anterior chamber. Daily injections of tuberculin in the same maximal doses were continued in the desensitized animals. In some of these experiments, the R 1 controls were given injections of broth in doses equivalent to the injections of tuberculin. In others, the R 1 controls received injections of glycerin in salt solution, since tuberculin contains approximately 25 per cent glycerin. In still others, the R 1 controls received no daily injection. Approximately twice a month the allergy to tuberculin of the three groups of animals—the normal controls (now infected with virulent bacilli), the R 1 controls and the desensitized animals—was tested by intracutaneous injection of tuberculin. The results of these tests showed that the desensitized guinea-pigs remained desensitized, the normal controls became allergic to tuberculin nine days after the injection of virulent bacilli, the untreated R 1 controls and those treated with glycerin remained sensitive throughout the experiment, but the R 1 controls

treated with broth gradually lost their allergy, though not to a degree comparable with that of the guinea-pigs desensitized to tuberculin. Animals were observed for as long as three months following the injection of virulent organisms; the survivors were then killed.

The results of these experiments have many aspects of interest. The detailed results in regard to mortality from tuberculosis and in regard to the character and spread of the visceral lesions will be reported elsewhere. Here these results can be given only in summary. The mortality due to tuberculosis in the desensitized guinea-pigs was no greater than in the R 1 controls; only a few of either group died with widely disseminated tuberculosis within three months after the inoculation with virulent bacilli, whereas almost all the normal controls died in from four to seven weeks after infection and showed extensive visceral lesions. The spread of the visceral tuberculosis in the desensitized animals was, in general, somewhat less than in the R 1 controls. We may conclude, then, that so far as these two criteria of immunity are concerned, the loss of allergy was not associated with any loss of immunity. On the contrary, the resistance of the desensitized animals was, if anything, better than that of the R 1 controls.

REACTION IN THE EYES

In order to record graphically the severity of the infection, we have recorded at each examination the severity of the following symptoms: congestion and edema of the conjunctiva; congestion and exudate or tubercle formation on the iris; constriction of, and exudation into, the pupil; turbidity of the aqueous; opacity and vascularization of the cornea. Varying degrees of severity of each of these symptoms were recorded as from one to three or four plus. A sample of the type of record obtained on a single animal is shown in the table. The total number of plus marks for all the symptoms in a single eye were then added together. When these totals were averaged at each observation for each group of animals, a graphic representation of the progress of the disease in each group could be charted. The resulting curves were remarkably smooth even when small groups of from six to eight animals were used. The records obtained in this manner were found to have a high degree of objectivity. It was found, for instance, that other observers could be trained to make readings which checked accurately with those of the author. It seems worth while to emphasize the validity of this technic of recording the severity of a disease, since it could equally well be applied to the recording of other experimental and clinical problems.

The curves composed from different sets of animals belonging to the same group, e. g., R 1 controls, receiving comparable doses, were found to be strikingly similar in successive experiments, and when

different doses of organisms were given, the curves differed in characteristic ways. In figure 1 are shown the curves charted in this way on the course of the infection in six different groups of animals, each numbering six or more guinea-pigs, showing the effect of varying doses of organisms and of the presence or absence of previous immunization on the course of the infection. It may be noted that even with the smallest dosage used, a maximal reaction was obtained in the nonimmune animals, though this dosage produced no recognizable lesions in the immune animals. On the other hand, even the greatest dosage of organisms used failed to produce as rapidly progressive a lesion in the immune animals as the minimal dosage produced in the nonimmune group.

Normal Controls.—The reactions in the inoculated eyes of the three groups of animals exhibited most interesting characteristics. During the

Sample of Record Made on the Ocular Lesions Following Intra-Ocular Infection with Virulent Tubercle Bacilli

Date	Conjunctival Congestion	Conjunctival Edema	Congestion of Iris	Exudation of Iris	Pupillary Constriction	Pupillary Exudate	Corneal Opacity	Turbidity of Aqueous	Total
4/22.....	2	2	0	0	0	0	1	0	5
4/23.....	1	1	0	0	0	0	0	0	2
4/25.....	0	0	0	0	0	0	1	0	1
4/27.....	0	1	0	0	0	0	0	0	1
4/29.....	1	1	0	0	0	0	1	0	3
5/ 2.....	1	1	0	0	0	0	1	0	3
5/ 4.....	1	1	0	1	0	0	2	0	5
5/ 6.....	2	3	0	1	0	0	3	0	9
5/ 9.....	2	2	1	2	0	0	3	0	10
5/13.....	2	3	2	2	1	0	5	1	16
5/16.....	1	2	1	2	2	0	5	1	14
5/20.....	3	3	2	3	2	2	6	2	23

first twenty-four to forty-eight hours following the inoculation, the previously normal guinea-pigs showed slight conjunctival congestion and edema and a faint clouding of the cornea at the point of puncture. In a few instances, the iris was congested and the pupil contracted. Accidental infection with pyogenic organisms occurred in only about 2 per cent of these animals. After the subsidence of this initial traumatic reaction, which lasted not more than seventy-two hours, the eyes regained a normal appearance. The subsequent course depended only slightly on the dosage and on the virulence of the strain used. Within from ten to fourteen days after the injection, the eyes again became inflamed, and small yellowish-white nodules approximately 0.25 mm. in size appeared in the iris. The pupil was contracted, and an exudate developed in the pupillary zone with extensive synechia. The aqueous gradually became turbid; opacities at first nebulous then denser and more diffuse developed in the cornea, and were rapidly followed by vascularization. Within from three to five weeks after the injection, the whole anterior segment of the eye had become converted into a caseous

mass. Soon the cornea ruptured. The intra-ocular contents were discharged, and only a shrunken stump remained.

Histologically, the lesions are characterized initially by the formation of small tubercles on the iris and in the anterior portion of the ciliary body, and later on the posterior surface of the cornea. The tubercles grow and become conglomerate. About the third week after the injection, caseation of the tubercles takes place (fig. 2), and the whole anterior segment of the eye becomes filled with a plastic exudate consisting mainly in epithelioid cells and lymphocytes. The involvement of the posterior half of the eyeball is generally less intense.

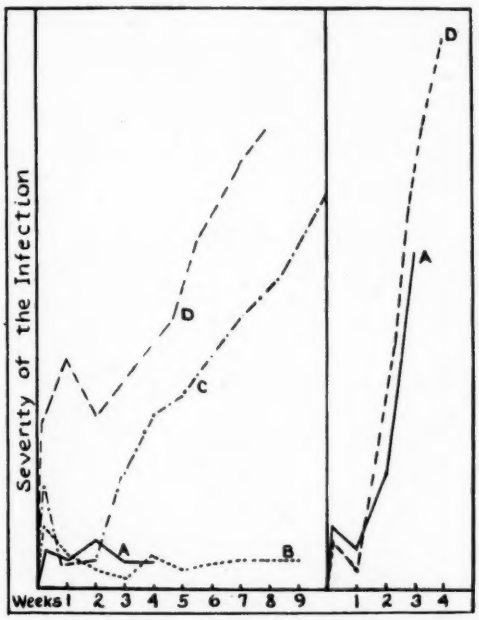

Fig. 1.—Curves illustrating the course of the intra-ocular infection in different groups of animals following the intra-ocular injection of different numbers of virulent organisms: on the left are the curves of the immune allergic animals (R 1 controls); on the right, of the previously normal animals (normal controls). Curves *A* show the results of injecting approximately 5,000 organisms; curves *D*, the result of injecting 0.005 cc. of a turbid suspension of organisms containing uncountable numbers of bacilli, and curves *B* and *C*, intermediate dosages.

This course of events is identical with that which has been frequently observed by other workers, and is presented merely as evidence of the efficacy of the inoculation.

R 1 Controls.—The R 1 controls exhibited, after virulent intra-ocular inoculation, a response which varied much more markedly with the variations in dosages used than did the normal controls. The immunity of these animals proved to be so high that they were able to

tolerate the injection of considerable numbers of virulent bacteria into the eye (approximately 25,000 organisms in one experiment) without showing any reaction beyond that determined by the trauma of the injection. This was the most concentrated suspension of tubercle bacilli that we could prepare free from clumps. When suspensions containing clumps of bacilli were injected, an initial acute inflammatory reaction developed. There were marked edema and congestion of the conjunctiva. The iris was congested and covered with a fine exudate. The pupil was contracted. Fine posterior synechiae were formed, and the aqueous often contained a fibrin clot. A diffuse haze of the cornea developed with stippling of the corneal reflex.

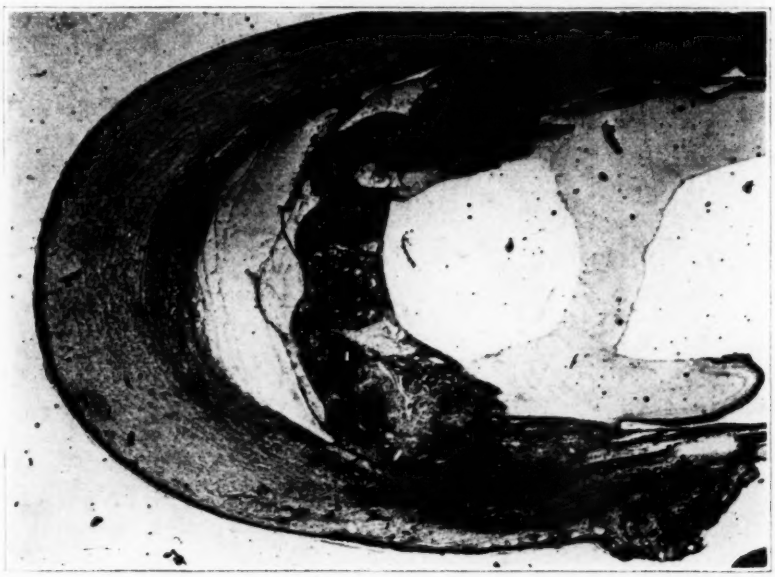

Fig. 2.—Beginning caseation of the iris and cornea in a nonimmune guinea-pig three weeks after inoculation of virulent bacilli into the anterior chamber.

With the smallest dosage capable of eliciting this initial allergic response, the acute reaction tended to subside in from two to four days, after which the eyes remained quiet for a week or more. Gradually, however, small grayish nodules appeared in the iris, associated with pericorneal congestion and flaky opacities in the cornea. The clinical picture at this stage was comparable to that of the common form of tuberculous kerato-iritis and scleritis in man. In some instances, the tubercles on the iris came and went. Occasional spontaneous cures were noted. On the whole, however, the condition was slowly but steadily progressive with increasing congestion of the eyeball, increasing opacity and vascularization of the cornea and increasing size and number of the tubercles in the iris.

When still larger doses of organisms were given, the initial allergic reaction assumed an even more severe form, and though some subsidence of the reaction was observed between the third and tenth day, the eyes never became free from symptoms, and a steadily progressive inflam-

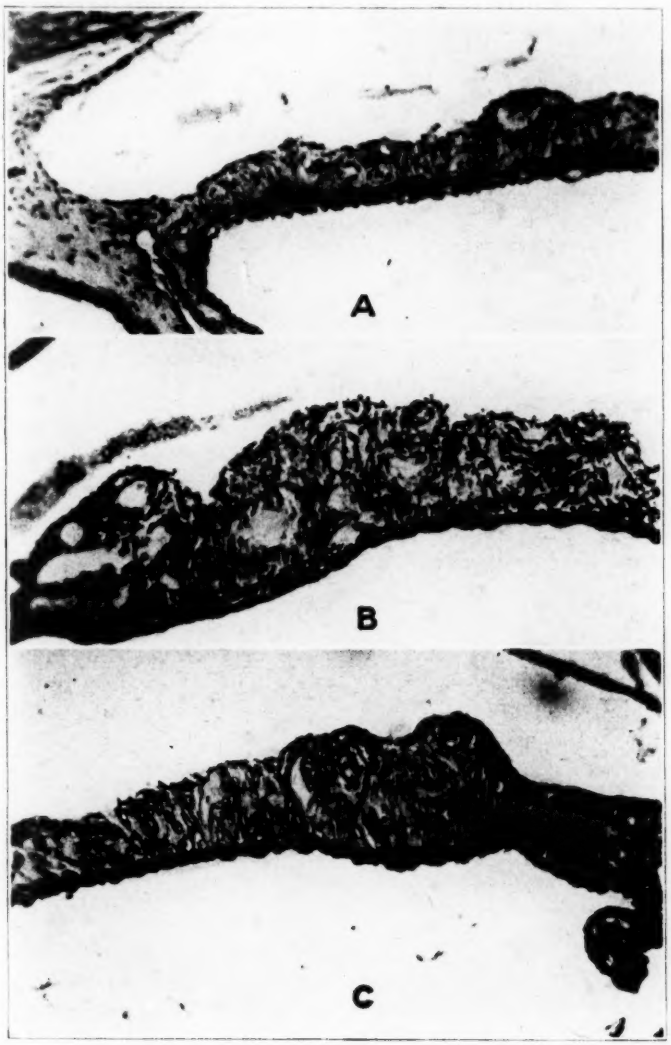

Fig. 3.—Reaction in the iris forty-eight hours after inoculation of virulent bacilli into the anterior chamber: *A*, nonimmune animal (normal control); *B*, immune allergic animal (R 1 control); *C*, desensitized immune animal. *A* and *C* show no reaction beyond that conditioned by the trauma, while *B* shows a diffuse cellular infiltration of the iris and a fibrin clot in the anterior chamber.

mation was observed at the end of this period of relative quiescence. The final state of many of these eyes was usually that of complete caseation of the whole anterior segment of the globe quite comparable to

that observed in the normal controls. It must, however, be emphasized that the normal controls reached this state of caseation in from three to four weeks when doses of organisms were used that produced no inflammation whatever in the R 1 controls, while even with maximal doses the latter required from six to twelve weeks to caseate and in many instances never progressed beyond the sluggish form of keratoiritis.

Histologic examination during the initial allergic response revealed an inflammatory exudate in the iris, ciliary body, anterior chamber and

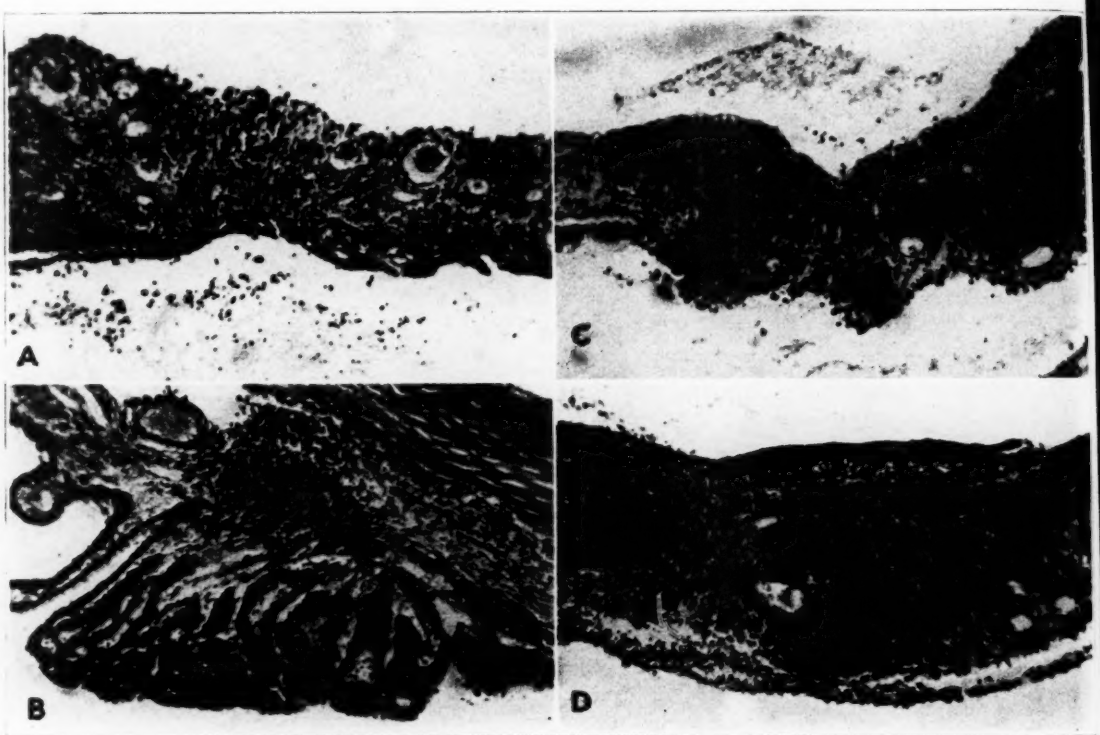

Fig. 4.—Varying stages of the intra-ocular reaction in immune allergic animals following the inoculation of virulent bacilli into the anterior chamber: *A*, diffuse infiltration of the iris with minimal tissue destruction or distortion; *B*, tubercle formation at the iris root with tissue distortion but without tissue destruction; *C*, tubercle formation in the iris with tissue destruction, and *D*, tubercle formation in the iris with beginning caseation.

cornea, which, twenty-four hours after inoculation contained about equal numbers of lymphocytes and polymorphonuclear leukocytes. After forty-eight hours, the polymorphonuclear leukocytes had for the most part disappeared, and in their stead large numbers of epithelioid cells were seen (fig. 3). Seventy-two hours after the injection, the reaction was usually less intense and the infiltration of the cornea less marked,

but the infiltration of the iris and ciliary body remained. In some instances, aggregates of epithelioid cells could be found on the pupillary margin of the iris forming the familiar "Koeppe" nodules. With the subsidence of the acute allergic response, the intensity of the infiltration decreased, but a few lymphocytes and epithelioid cells could generally be found near the iris root weeks later, even in eyes which clinically showed no abnormality.

The histologic picture of the progressive inflammatory reaction in these R 1 animals showed several easily recognizable stages. At first,

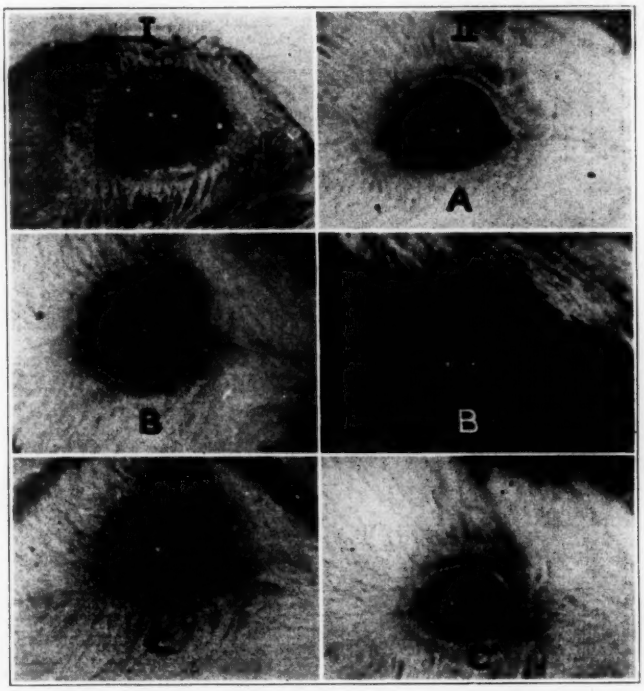

Fig. 5.—Eyes of guinea-pigs showing reactions of average severity following inoculation of the same volume of the same suspension of virulent tubercle bacilli into the anterior chamber. The upper two eyes are from nonimmune animals (normal controls); the two in the center, from immune allergic animals (R 1 controls), and the lower two eyes, from immune desensitized animals treated with tuberculin. The eyes in the column on the left were photographed three weeks after infection; those in the column on the right, six weeks after infection.

a diffuse epithelioid cell and round cell infiltration of the iris and anterior portion of the ciliary body appeared similar to that found in the late stages of the initial allergic response (fig. 4, *A*) Small epithelioid cell tubercles then developed in the iris and ciliary body. These tubercles seemed to lie loose in the stroma without producing any tissue destruction (fig. 4, *B*). Later, however, destruction and distortion of the

stroma developed (fig. 4, *C*). Similar tubercles now were frequently found in the cornea, sclera and episcleral tissues. As the tubercles grew, caseous foci appeared within them (fig. 4, *D*) which spread and became confluent until the whole anterior segment was filled with a caseous mass. Throughout the course of the infection, until rupture of the eyeball, the reaction in the choroid, retina and vitreous remained insignificant.

Desensitized Guinea-Pigs.—The reaction of the desensitized guinea-pigs can best be compared with that of the R 1 controls. When the number of organisms injected was insufficient to produce clinically visible lesions in the latter, the former also showed no reaction. With

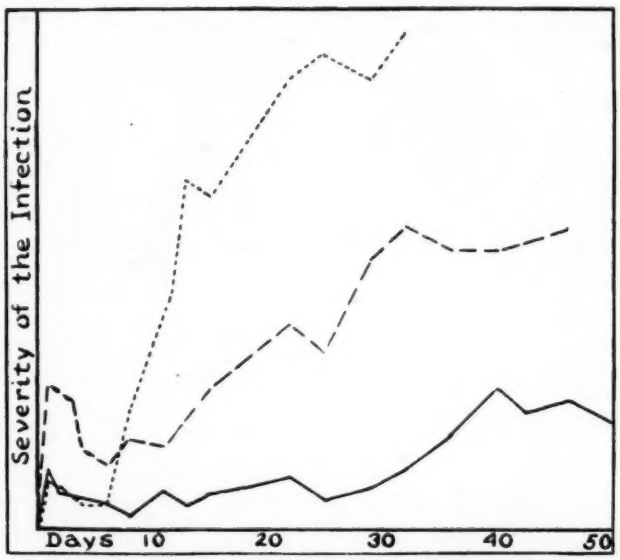

Fig. 6.—Graphic record of the severity of the disease following the intra-ocular injection of 0.005 cc. of a suspension of virulent tubercle bacilli into the anterior chambers of each of three groups of guinea-pigs. Each curve represents the average reaction of thirty or more guinea-pigs. All animals included in this chart were inoculated with the same suspension of organisms on the same day. The dotted line shows the reaction of nonimmune animals (normal controls), the broken line that of immune allergic animals (R 1 controls) and the solid line that of immune desensitized animals (treated with tuberculin).

a dosage sufficient to produce a severe initial allergic reaction and a progressive ocular tuberculosis in the R 1 controls, little or no initial reaction occurred in the desensitized animals, and the subsequent course of the inflammation showed less tendency to progress and reached a less severe final stage than that in the corresponding R 1 controls. Many of these animals never showed ocular lesions. With massive doses of organisms a mild initial allergic response was elicited in some of the desensitized animals. It is evident that even with the heroic

injections employed complete desensitization could not be achieved. However, the dosage of organisms required to elicit an allergic response in these animals was far greater than that occurring in the tissues even in rapidly progressive tuberculosis. The initial allergic response, when present, was of considerably less severity than that found in the corresponding R 1 controls, and the subsequent course of the disease was likewise less severe; caseation of the anterior segment with rupture of the cornea occurred in only a small number of this group. Figure 5 shows the eyes with lesions of average severity in each of the three experimental groups taken three and six weeks after inoculation with virulent bacilli. Figure 6 represents the graphic record of the severity of the ocular reaction in an experiment performed as outlined.

The histologic features of the reactions in the desensitized animals taken as a whole showed the same stages as those found in the R 1 controls. When, however, eyes showing the same degree of clinical severity in the two groups were compared, it was found that the desensitized animals on the whole showed less tendency to develop tissue destruction and caseation about their intra-ocular tubercles than did the R 1 controls.

CONCLUSIONS

1. Practically complete desensitization of tuberculous guinea-pigs can be achieved by daily injections of massive doses of tuberculin.

2. Guinea-pigs immunized to tuberculosis and sensitized to tuberculin by inoculation with an avirulent strain of tubercle bacilli, and subsequently desensitized to tuberculin, show no diminution in their resistance to reinfection as tested by the mortality of the disease, the spread of the infection or the progress of the local lesion. In all these respects, the desensitized animals showed more resistance to reinfection than did nondesensitized controls. Allergy in tuberculosis cannot be regarded as essential to immunity.

3. The rationale for the use of tuberculin in treating tuberculous infection is, therefore, the production of perifocal desensitization rather than perifocal allergic reactions.

4. When sufficient numbers of tubercle bacilli are injected into the anterior chambers of guinea-pigs immune to tuberculosis and allergic to tuberculin, an acute fibrinous iridocyclitis is produced which usually subsides in from two to four days. This reaction is anologous to the Koch reaction in the skin.

5. The clinical picture of tuberculous kerato-iritis as seen in human beings can be reproduced in guinea-pigs by the inoculation of living tubercle bacilli into the anterior chambers of animals previously immunized by subcutaneous injection of avirulent organisms. Similar

inoculation of nonimmune animals produces a rapidly caseating lesion unlike anything seen clinically in human beings.

6. Partial desensitization of guinea-pigs allergic to tuberculin can be achieved by daily massive injections of sterile glycerin broth.

ABSTRACT OF DISCUSSION

DR. W. H. WILMER, Baltimore: We have found by clinical experience that those patients who have done best are those who have been desensitized. The patients in whom we have not gotten good results still remain rather sensitive to tuberculin. Those patients that have gotten well without any reaction have not shown a marked degree of sensitivity to tuberculin.

DR. JONAS S. FRIEDENWALD: The results in these experiments support the idea that the mode of treatment to be desired in the tuberculous patient is desensitization, and it seems to me that the general plan of treament which Dr. Wilmer has published is that which fits this rationale best.

DARK ADAPTATION IN THE ALBINOTIC EYE

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The occurrence of pigmentation in conjunction with visual function, from the most primitive photoreceptors to the complex mammalian eye, suggests that pigments form an integral part of the physiology of vision.[1a] Schanz, making use of the known photo-electric effects of fluorescent dyes, based his theory of vision on the absorption of light by the pigment of the pigment epithelium of the retina, which was assumed to emit electrons, thus stimulating the rods and cones.[2] Zikulenko considered the cells of the retinal pigment epithelium to be the primary visual elements, rather than the rods and cones.[3] Eldridge-Green based his theory of vision on the visual purple (rhodopsin) present in the rods.[4a] The photochemical changes involved in dark adaptation have likewise offered a field for speculation as to the possible rôle of pigments of the eye as photosensitive or light-absorbing substances.

The general course of dark adaptation, measured by determinations of minimum intensities perceptible at succeeding stages, has been well established by numerous systematic investigations, beginning as early as 1865 with that of Aubert.[5] Improvement in technic of physical measurement and a clearer understanding of some of the physiologic factors causing individual variation have made more accurate studies possible. However, much of the data regarding the nature of the photochemical changes of dark adaptation is based entirely on indirect evidence.

Wölfflin,[6] in 1905, suggested that the speed of adaptation might depend partly on the pigment content of the retina, since he considered the process to be slower in blondes than in dark subjects. If observable

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From the Howe Laboratory of Ophthalmology, Harvard University, and the Massachusetts Eye and Ear Infirmary.

1. Adler, F. H.: (*a*) A Comparative Study of the Rôle of Pigment in the Physiology of Vision, Arch. Ophth. **57**:347 (July) 1928; (*b*) p. 353.

2. Schanz, F.: A New Theory of Vision, Am. J. Physiol. Optics **4**:284, 1923.

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5. Aubert, cited by Adams.[27b]

6. Wölfflin, E.: Der Einfluss des Lebensalters auf den Lichtsinn bei dunkeladaptiertem Auge, Arch. f. Ophth. **61**:524, 1905.

pigmentation is a significant factor in the measurement of the course of adaptation, it should be taken into consideration in determining the normal range among subjects. Provided that pigmentation in itself contributes to the sensitivity of the human retina under conditions of dark adaptation, a study of the changes in the albinotic eye should show obvious deviations from the normal, since pigment, if not entirely lacking in the true albino, is certainly poorly developed.

Comparatively few albinos have been tested for dark adaptation, their low incidence in the general population contributing to the difficulty of obtaining them as subjects. Schirmer [7] (1890), in a study of the validity of Weber's law for light sense, included four young albinos among his observers, and considered that their adaptation as tested by the Forster photometer was normal. Stargardt [8] (1910) mentioned that albinos have normal adaptation, and Pearson, Nettleship and Usher [9a] (1913) stated that "There is at present no reason to believe that either perception of color or light is defective in albinos." They reported two cases of night blindness in albino subjects, but considered them atypical. Mosso [10] (1914) found no influence of pigmentation on dark adaptation in his cases, and found normal adaptation in four albinos. Takagi [11a] (1926) made a number of tests of dark adaptation with two albino subjects, using a Nagel adaptometer, for the purpose of showing that migration of retinal pigment in man is probably not a part of the adaptation process. He likewise reported a normal rate and degree of adaptation. Thus, in the albinos whose light sense has been tested and described in the literature, no cases are found in which adaptation is defective. On the other hand, the popular myth that the albino sees better at night than the normal person apparently has no substantiation, as, grossly at least, the curve of adaptation in albino eyes is similar to that for normal eyes, showing a rapid initial increase in sensitivity followed by a more gradual change.

Pearson, Nettleship and Usher, in their study of albinism in man, defined complete albinism of the eye as existing "in those cases where

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7. Schirmer, O.: Ueber die Gülligkeit des weberschen Gesetzes für den Lichtsinn, Arch. f. Ophth. **36**:121, 1890.

8. Stargardt, K.: Ueber Störungen der Dunkeladaptation, Arch. f. Ophth. **73**:77, 1910.

9. Pearson, K.; Nettleship, E., and Usher, C. H.: (*a*) A Monograph on Albinism in Man, London, Dulau & Co., 1911-1913, pt. 2, p. 293; (*b*) p. 268; (*c*) p. 271; (*d*) p. 273; (*e*) p. 274; (*f*) p. 270; (*g*) p. 300; (*h*) p. 275; (*i*) p. 329.

10. Mosso, G.: Il senso luminoso negli albini e l'influenza del pigmento retinco sulla sensibilità luminosa e sull' adattamento dell' organo visivo all' oscura, Ann. di ottal. e clin. ocul. **43**:79, 1914; abstr., Zentralbl. f. d. ges. Ophth. **1**:434, 1914.

11. Takagi, R.: (*a*) Dunkeladaptation bei Albinos und eine kurze Abhandlung über das Wesen der oguchischen Krankheit, Ztschr. f. Augenh. **58**:436, 1926; (*b*) p. 437, table 1.

the eye structures are entirely devoid of pigment." [9b] Such cases have been demonstrated in animals, but only a few microscopic studies of human albinotic eyes have been made, and in the majority of these there have been traces of subnormal pigment in some part of the eye. In 1784, Buzzi [12] published an account of his dissection of an albinotic eye, in which he found no traces of pigment. Wharton Jones,[13] in 1833, stated that the cells of the retinal epithelium of albinotic eyes are smaller and more rounded than those in the normal eye, but Usher [9c] later described the cells as normal in size and shape. Manz [14] (1878) gave a fairly complete histologic study of a pair of albino eyes which he obtained post mortem, in which the choroid, ciliary body and iris were without pigment, but the retinal epithelium showed weak pigmentation from the fundus to the back of the iris. In 1910, Adler and McIntosh [15] examined the organs of an albinotic infant (aged 10 weeks) and reported no trace of pigment in any part of the eye. Elschnig [16] and Usher,[9d] like Manz, found the pigment epithelium of the iris, ciliary body and retina, in their cases, to be pigmented, though they reported no pigment in the iris stroma, choroid or ciliary body. Brücke [17] found no pigment in any part of an albinotic eye, but Velhagen [18] detected it in the epithelium of the iris and the ciliary body in his case, and Gilbert [19] reported it in the pigment epithelium of the retina in his case. In portions of iris removed in cataract extraction in albinotic patients, Nettleship [20] found no pigment in his two cases, while Usher, in a single case, reported pigment in the posterior epithelium.

Though some traces of pigment in the retinal epithelium were reported in four of the nine studies which included this portion of the eye, in no case was the pigment as abundant as in the normal eye.

The pigment epithelium, with its single layer of pigmented cells, although associated with the choroid, arises, like the retina, from neural ectoderm. The choroid develops from associated paraxial mesoderm.[21a] In the normal human eye, pigment appears in the pigment epithelium of

12. Buzzi, M.: Opuscoli scetti, Milan, 1784; cited by Pearson, Nettleship and Usher.[9a]

13. Jones, Wharton, cited by Pearson, Nettleship and Usher.[9a]

14. Manz, W.: Ueber albinotische Menschenaugen, Arch. f. Ophth. **24**:3, 1878.

15. Adler, J. E., and McIntosh, J., cited by Pearson, Nettleship and Usher.[9a]

16. Elschnig, A.: Zur Anatomie des menschlichen Albinoauges, Arch. f. Ophth. **84**:401, 1913.

17. Brücke, E., cited by Manz.[14]

18. Velhagen, cited by Takagi.[11a]

19. Gilbert, W.: Ueber Pigmentanomalien des Auges, Arch. f. Augenh. **88**: 143, 1920.

20. Nettleship, cited by Takagi.[11b] Pearson, Nettleship and Usher.[9e]

21. Mann, Ida: (*a*) Development of the Human Eye, New York, The Macmillan Company, 1928, p. 17; (*b*) pp. 199 and 200; (*c*) p. 202; (*d*) p. 33; (*e*) p. 121; (*f*) p. 227; (*g*) p. 271.

the retina between the fourth and fifth week of embryologic development, being well developed by the time the embryo has reached a length of 10 mm.[21b] The pigment cells (chromatophores) of the choroid cannot be recognized until the fifth month of development.[21c] Pigmentation of the choroid begins near the sclera, in the outer layer, and spreads inward, toward the pigment epithelium, the pigment cells remaining more numerous near the sclera throughout life. At the third month, the posterior pigmented layers of the iris develop.[21d] The anterior layer of the iris epithelium is continuous with the pigment layer of the retina (the outer wall of the optic cup), and the posterior layer of iris is continuous with the inner wall of the optic cup; at the third month, only the cells of the anterior layer are pigmented, the cells of the posterior layer becoming gradually pigmented between the third and seventh months.[21e] Pigmentation spreads no farther even in adult life. The iris stroma, arising from the same tissue as the choroid (mesoderm), is generally without pigment at birth, the pigmentation occurring to a variable extent in postnatal [21f] life, the blue appearance of the iris in the new-born being due to the pigment epithelium on the posterior surface of the iris. In some eyes, no observable pigment ever develops in the iris stroma, and the color remains blue or grayish, depending on the thickness of the iris.

In the lower vertebrates, the processes of the pigment epithelium pass between the outer limbs of the rods and cones,[21g] and here migration or phototropic shifting of the pigment is easily demonstrated in frogs, which have large rods in comparison to warm-blooded animals.[22a] No displacement of pigment has been demonstrated in man. The assertion of Nakamura that the displacement of the retinal pigment plays an important rôle in dark adaptation influenced Takagi [11a] to test two albinos. The normal curves which he obtained for persons without visible retinal pigment seem to indicate that Nakamura's assumption is erroneous.

The normal pigmentation of the retinal epithelium in man shows rod or spindle-shaped granules, and Raehlmann described also small light yellowish bacterial rods. A protoplasmic substance, reddish in the darkened eye of an animal, may bind together several rods of pigment to make up some of the "fucin" needles. This substance bleaches in the light just as visual purple does, and Raehlmann considers it identical with the visual purple. The fact that visual purple, the transparent red coloring matter present in the outer members of the rods, will regenerate only as long as it remains in contact with the retinal epithelium would seem to indicate a close relationship between the photosensitive visual

22. Salzmann, M.: (*a*) The Anatomy and Histology of the Human Eyeball in the Normal State, Its Development and Senescence, translated by E. V. L. Brown, Chicago, University of Chicago Press, 1912, p. 61; (*b*) chaps. 6 and 7.

purple and the pigment epithelium. The visual purple, rhodopsin, cannot be observed ophthalmoscopically because the red coloring of the fundus obscures it.[22b] It can be seen in the fresh retinas of eyes that have previously been kept in the dark. Visual purple has been demonstrated in the retinas of the human fetus,[4b] and the agreement between the scotopic (twilight) luminosity curve and the absorption curve of visual purple indicates that this photosensitive substance is certainly present in the human eye. In fact, the curves for absorption of visual purple and bleaching of visual purple and the luminosity curve for the dark-adapted eye are analogous, as pointed out by Henri and des Bancels,[23] and support the assumption that the regeneration of visual purple is the real basis of dark adaptation. Visual purple is probably present in all animals that have rods. It is present in albinotic animals, having been demonstrated in rabbits.[4b] As Adler pointed out,[1b] the experiments of Takagi, showing normal adaptation in albinotic eyes, do not exclude the presence of visual purple even though pigmentation is defective. Dittler,[24] in a review of the objective changes of the retina under the influence of light, stated that the pigment epithelium probably has a secretory function in connection with the generation of visual purple, but because regeneration of visual purple occurs in albinos, no significance is assigned to the presence or absence of pigment in the process of dark adaptation.

In the albinotic eye, sometimes described as a developmental anomaly, the pigments of the retinal epithelium, of the posterior layers of the iris and of the choroid, as well as of the iris stroma, may fail to develop. Nettleship described, as his criterion of ocular albinism, a "lack or deficiency of the retinal epithelial pigment."[9f] He had the opinion that the quantity, not the color, of the pigment in the retinal epithelium may be practically constant in all normal eyes regardless of differences in pigment of the choroid and iris. He considered microscopic evidence in favor of this view, at least for European eyes, but stated that the degree of pigmentation is generally assumed to vary directly as that of the choroid.[9g]

Clinically, the albinotic eye[9h] usually presents a reddish pupillary reflex due to circulation in the choroidal vessels, which are clearly visible ophthalmoscopically. The brightness and direction of the light, the thickness of the iris and the size of the pupil are factors which may affect the color of the pupil. The iris is often sufficiently translucent to appear gray in the proper light, though it may absorb so much of the

23. Henri and des Bancels, quoted by Adams.[27e]

24. Dittler, R.: Photoreceptoren, in Bethe, A.; Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie mit Berücksichtigung der experimentellen Pharmakologie, Berlin, Julius Springer, 1929, vol. 12, p. 291.

light returning from the back of the eye that it appears blue or violet. Ophthalmoscopically, one cannot detect pigment in the retinal epithelium of the albino, and if traces are present, they can be demonstrated only microscopically.

Certain other characteristics of the albino eye, aside from a lack of pigment, are to be noted. Aplasia of the fovea, with a lack of the yellow coloring found in the macula of the normal eye, has been demonstrated. In 1838, Carron du Villard examined two preserved albino eyes which showed no trace of the yellow spot. Manz reported no yellow color in the macular region of the retina in his specimen. However, Buzzi's and Usher's specimens had normal macular coloring.[9h] Fritsch found the fovea imperfectly developed and the yellow spot not macroscopically distinguishable in the eye of an African albino. Ichikawa,[25] in a clinical study of the ophthalmoscopic appearance of the fovea in albino eyes, reported that the fovea could not be differentiated in any of his cases except one, in which there was myopia of 14 diopters and the macular region had a grayish appearance. Elschnig also reported a complete lack of a fovea centralis in the albinotic eye, the center of the retina not having the high differentiation typical of the normal eye. The fovea takes its definite structure during the first month of life, probably under the influence of light, but in the albinotic eye this development fails to occur, the retina apparently retaining a lower stage of development. High refractive errors characteristic of the albinotic eye are usually complicated by various forms of astigmatism, simple hyperopia and myopia being more rare, and emmetropia being almost unheard of in the albino. Nettleship reported a case of emmetropic refraction in a young albino with a visual acuity of 6/60 in both eyes. Horizontal or rotary nystagmus, usually with rapid oscillations (from 100 to 150 per minute), is almost invariably present. Poor vision is thought to be due principally to the deficiency of pigment in the retinal epithelium. Whatever the functions of this layer of the retina may be, it is essential to good vision. A lack of pigment, of course, causes the albinotic eye to suffer from an excess of diffused light, which enters not only through the translucent iris (which is still more translucent with a small pupil because the iris is then thinner), but on all sides through the sclera and unpigmented choroid. It would be difficult to obtain clear images under such circumstances because of a lack of contrast.

EXPERIMENTAL DATA

It is the purpose of this study to compare the course of dark adaptation of a group of albinotic eyes having defective pigmentation with that of a group of eyes in which pigmentation can be considered normal.

25. Ichikawa, K.: Ueber den ophthalmoskopischen Befund der Area centralis des albinotischen Auges, Klin. Monatsbl. f. Augenh. **51**:84, 1913.

It is immediately evident that the ocular symptoms accompanying albinism, aside from weak pigmentation, must not be ignored, and comparison with normal eyes must take into consideration the fact that varying degrees of nystagmus were present in all the albinos tested and all had refractive errors, with low visual acuity, averaging probably 20/200 with correction.

Twelve albinos were tested, ten of whom (five boys and five girls) were used for the study, the remaining two being too young to give satisfactory results. The ten subjects used ranged in age from 13 to 21 years, the average age being 16½ years. Nine of the subjects had typical albinotic hair (white) with white lashes and brows and bluish irides; one subject who had typical albinotic eyes with white lashes had red hair. (Nettleship [91] discussed the frequent association of red hair with albinism, stating that microscopic examination of red hair indicates that it can be as free from granular pigmentation as the whitest of albino hairs.) All ten subjects had nystagmus, low visual acuity and more or less photophobia in the sunlight, most of them wearing lightly tinted lenses. Six were tested without glasses, three with untinted glasses and one with lightly tinted glasses.

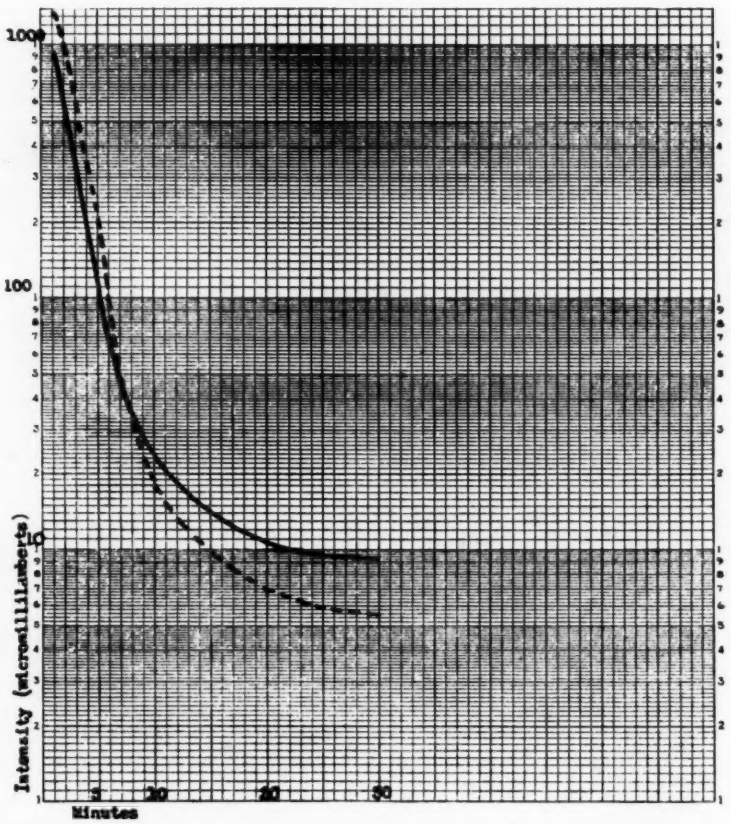
In the normal group, thirteen adults were tested, some of whom had refractive errors corrected with glasses. Data from these subjects were used as typical of the normally pigmented eye.

A Nagel adaptometer was used to follow the course of adaptation for half an hour, with monocular observations after one, five, ten, twenty and thirty minutes in the dark. One observation for each eye was taken at one minute, and the average of two observations for each eye was taken at each of the following intervals, when the change in sensitivity was no longer so rapid as during the first minute. Each subject was adapted to light for five minutes before the test, a preexposure screen illuminated with two 100 watt bulbs (the illumination value of the screen was 18.59 millilamberts) being used, in order that all might start the test from the same level of adaptation. Observations followed one minute after the screen was removed. A chin rest 114 cm. from the 10 cm. test spot was used to orient the observer, and to assure the maintenance of the proper distance to give a 5 degree circular field. The illumination values of the adaptometer were calibrated with a Macbeth illuminometer. The micromillilambert (one millionth of a millilambert), a unit employed in previous light test work at the Massachusetts Eye and Ear Infirmary in order to eliminate decimals, was used.[26] The calibration was checked from time to time; a decrease in brightness from a possible deterioration of the light source (three 100 watt seasoned

26. Waite, J. H.; Derby, G. S., and Kirk, E. B.: The Light Sense in Early Glaucoma, Particularly the Achromatic Threshold at the Macula, Tr. Ophth. Soc. U. Kingdom **45**:311, 1925.

Mazda daylight bulbs) could be compensated for by increasing the current controlled by a rheostat. Curves showing the course of adaptation could be easily plotted on semilogarithmic paper, the arithmetical abscissae being used for the time in minutes, and the logarithmic ordinates for the intensity in micromillilamberts (chart).

Because of the variation in retinal sensitivity from the fovea to the periphery, in order that approximately the same retinal area might be used by the normal observers, a 1 cm. red cross, placed 0.5 cm. above



Average curves of normal persons and of albinos. The continuous curve indicates the normal average; the broken curve, the albino average.

the test field, was used as a fixation point. (A red Tscherning photometric glass filter, no. 6, passing only long wavelength light, was used for the fixation point. This light is supposedly ineffective for stimulation of the rods;[27a] hence, no measurable adaptation occurs to red light, and foveal fixation is easily maintained.) The refractive errors and

27. Adams, D.: (*a*) Dark Adaptation, Medical Research Council, Special Report Series, no. 127, London, His Majesty's Stationery Office, 1929, p. 31; (*b*) p. 6; (*c*) p. 95; (*d*) p. 42; (*e*) pp. 55 and 56; (*f*) pp. 94 and 95; (*g*) p. 97.

nystagmus of the albinos prevented them from holding fixation, and the fixation point could be used only for the normal subjects. Thus, for the albinos the part of the retinal field used cannot be determined. Rapid nystagmic movements probably mean that the albino has, in effect, a larger retinal field exposed to the light test spot than the person who is able to fixate.

Since I am not dealing with persons having abnormalities of the pupil from disease, senility or the use of miotics or mydriatics, I have, for the purpose of this study, assumed that pupillary changes were a constant factor. Unless one is interested in the measurement of the exact retinal illumination, which Hecht calculates in photon units,[27d] comparison of groups of observers is just as valid on the basis of natural pupillary size (provided the pupillary changes are normal) as on the basis of some arbitrarily chosen width of the pupil obtained by the use of an artificial pupil or by correction factors such as those furnished by Reeves' photographic data [28] on the change in the size of the pupil. The use

TABLE 1.—*Increase in Sensitivity in Dark*

	Average Intensity, Micromillilamberts		Standard Deviation of Distribution	
Minutes in Dark	Normal Subjects	Albinos	Normal Subjects	Albinos
1	937.9	1,336.9	513.7	989.9
5	124.5	199.4	78.6	226.8
10	22.4	17.5	8.8	11.5
20	10.6	6.8	5.4	3.2
30	9.2	5.5	5.5	3.9

of a miotic, as in previous test work on light at the Eye and Ear Infirmary, with its accompanying discomfort and possible effect on adaptation itself [27e] and the likelihood of small errors in measurement of the contracted pupil, did not seem warranted. The use of the normal pupil with its slight individual differences in the rate of opening and closing [28] is more convenient, and probably not less accurate. Reeves' data could be employed if it seemed useful to reduce the data of the tests to a given pupillary width.

In a comparison of albinotic and normal adaptation, the average results for the two groups, rather than individual curves, have been used. The accompanying chart gives the average curves for the two groups, the illumination values being given in table 1. The illumination values represent average threshold sensitivity, obtained by increasing the brightness of the test spot until it was just visible. Sensitivity to light, not form (of the test spot), was measured. The values in table 1 show, grossly, that the albinos as a group are at first less sensitive than normal subjects, the average minimum intensities visible after the one

28. Reeves, P.: Rate of Pupillary Dilation and Contraction, Psychol. Rev. **25**:330, 1918.

minute and five minute periods being higher for the albinos than for the other group. However, for the remaining three periods, the average minimum intensities are lower for the albinos than for the normal subjects, indicating that after ten minutes or longer in the dark, the albino is more sensitive to low illumination than the normal subject.

Since the groups studied are small and the individual variations in adaptation are quite large, as shown by the standard deviations given in table 1, the apparent differences between the normal subject and the albino might be due to a chance selection of cases. However, there is no reason to assume that the samples are not representative of all normal persons and all albinos, though the albinos were somewhat younger than the normal subjects tested. Table 2 gives the differences between average minimum intensities for the normal subjects and for the albinos at each time interval, the standard deviation of the difference and the ratios of these values. A ratio of 3 or over indicates a completely reliable difference, meaning that further testing of other groups

TABLE 2.—*Differences Between the Intensity Values for Normal Subjects and Albinos, the Standard Deviation of the Difference and the Ratio Between These Values*

Minutes in Dark	Differences	Standard Deviation of Difference	Ratio
1	399.0	243.10	1.64
5	74.9	52.90	1.41
10	4.9	3.00	1.63
20	3.8	1.28	2.96
30	3.7	1.40	2.64

of normal subjects and albinos under the same conditions is practically certain to give approximately the same difference in averages. The ratios may be interpreted as follows in terms of "chances that the obtained difference represents a true difference greater than zero:" [29]

Minutes in the Dark	Ratio	
1	1.64	94 chances per hundred that any albino is less sensitive than a normal person after one minute in the dark
5	1.41	92 chances per hundred that any albino is less sensitive than a normal person after five minutes in the dark
10	1.63	94 chances per hundred that any albino is more sensitive than a normal person after ten minutes in the dark
20	2.96	99.9 chances per hundred that any albino is more sensitive than a normal person after twenty minutes in the dark
30	2.64	99.6 chances per hundred that any albino is more sensitive than a normal person after thirty minutes in the dark

All the differences, as shown, are sufficiently large to insure a nine to one chance that the differences found in the experimental groups would be approximated if other groups of normal subjects and albinos were tested under the same conditions and the results compared.

29. Garrett, H. E.: Statistics in Psychology and Education, New York, Longmans, Green & Co., 1926, chap. 3, sect. 4, p. 128.

Comparing the general course of adaptation in the two groups, it can be stated that the albinos are at first slower in adapting than normal persons, but after ten minutes they overtake them, and by twenty or thirty minutes, they may surpass normal persons, being somewhat more sensitive to low illuminations. On the whole, the two curves (chart) are so similar that it is reasonable to assume that the active element in dark adaptation is present in both groups of eyes, regardless of whether or not pigmentation is normal. This element is probably visual purple, which has been demonstrated in albinotic animals, and is undoubtedly present in the human albino. Pigmentation as such thus appears to play no necessary part in the process of dark adaptation. Any possible secretory function of the pigment epithelium in the production of visual purple is evidently served equally well when there is no deposit of actual pigment in the epithelium. The colorless *Vorstufe* of the pigment, described in embryologic development, is perhaps sufficient in the albino eye.[30]

It is, however, necessary to explain why the average albino curve is not identical with the average normal curve. Visual purple is bleached rapidly on exposure to light,[27f] and is reformed when the retina is exposed to darkness. Müller [31] suggested that the reformation was at first slow because of the precursor substances formed by bleaching. Thus, the more thorough the bleaching, the slower is the beginning of dark adaptation. The visual purple in the albinotic eye with its lack of pigmentary protection (translucent iris and defective choroidal and retinal pigment) was probably more completely bleached than the normal eye on preexposure to light. Consequently, the reformation of visual purple occurred more slowly at first in the albinos, showing a less rapid initial rise in sensitivity than was found in the normal subjects. However, after ten minutes or more in the dark, the original retardation is overcome and the albino eye is then measurably more sensitive to low illuminations than the normal eye. One would expect the albinos to be somewhat more sensitive on the basis of age, Walker and others having demonstrated that young persons adapt somewhat more readily than adults.[32] Moreover, the lack of fixation in the albinotic eye might account for its apparent greater sensitivity after adaptation has occurred. Certainly, nystagmic movements prevented confining the testing to a single part of the retina.

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30. Schieck, F., and Brückner, A.: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, 1930, vol. 1, p. 489.

31. Müller, cited by Adams.[27g]

32. Walker, W.: Ueber die Adaptationsvorgänge der Jugendlichen und ihre Beziehungen zu den Transformationserscheinungen, Ztschr. f. Psychol. **103**:323, 1927.

SUMMARY

Dark adaptation in twenty albino eyes was compared with that in twenty-six normally pigmented eyes. Curves for the two groups, while essentially similar and probably dependent on the formation of visual purple in both normal persons and albinos, showed certain differences: The albinos adapt less rapidly at first, but become somewhat more sensitive than the normal subjects after ten minutes in the dark, and continue to be somewhat more sensitive up to the end of the thirty minute test. Lack of normal pigmentation in the albino eye, while it may be the physical factor causing the initial retardation in the albino sensitivity, because of greater bleaching of visual purple in the pre-exposure to light, does not prevent the progress of dark adaptation.

INTRACAPSULAR EXTRACTION AT THE GERMAN EYE CLINIC (ELSCHNIG) IN PRAGUE

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That intracapsular extraction of a cataract is a well established procedure there is no doubt, but the fact that it is far from a settled question and one that is still frowned on by many operators prompted me to report on the operation.

The following is a report of the cases seen by me during my stay at Professor Elschnig's clinic in Prague, along with a brief outline of the technic used.

A few words might be profitably said as to the care of patients before operation. As a routine, the following procedures are carried out in all cases of cataract: Irrigation of the lacrimal apparatus is performed to detect any pathologic process. Two sterile cultures in serum bouillon, on successive days, must be obtained from the conjunctival sac before operation. Two or three days before operation oxycyanide of mercury, 1 : 5,000, is instilled into the eye every hour. At night a salve of oxycyanide, 1 : 5,000, is used.

As a sedative, a powder with the following formula is given from one to two hours before operation:

	Cc. or Gm.
Codeine sulphate	0.02
Sodium bromide	0.05
Sodium salicylate	0.50

Venesection is performed on all patients with a systolic blood pressure over 150. This is done just before the operation.

When the patient is ready for operation, the cilia of the upper and lower lids are cut, and the pupil is dilated with homatropine, 1 per cent. The lids are painted with iodine, 5 per cent, and akinesia is obtained by the infiltration of procaine hydrochloride, 2 per cent, with epinephrine into the orbicular muscle outside the margin of the orbit. Care is taken not to cause infiltration of the lids. Cocainization is done in the usual way with 3 per cent cocaine in a 1 : 5,000 solution of oxycyanide of mercury, which is boiled just prior to the operation.

After waiting ten minutes, the eye is irrigated with a 1 : 10,000 solution of oxycyanide of mercury by means of a rubber balloon and a metal cannula.

Retrobulbar injection is made with the same procaine hydrochloride solution. The needle, which is 5 cm. long, is pushed through the skin of the lower outer margin of the orbit, so as not to pierce the conjunctiva. It continues back in the orbit till the base of the needle is reached; 1 cc. is injected at this point. The eye is then compressed firmly through the closed lids for three or four minutes. This precaution is taken to prevent exophthalmos from retrobulbar hemorrhage. Then a bridle suture of white silk is placed through the superior rectus tendon. An assistant holds the lids by Desmarre's lid holders and also controls the bridle suture.

The globe is fixed by means of Elschnig's fixation forceps, which are placed near the limbus at 7 o'clock in the left eye and at 5 o'clock in the right eye; it should be realized that the patient is operated on in bed, and that the operator sits on the bed, facing the patient. This also means that the operator must be adept with both hands.

The incision is made in the usual manner with the Graefe knife, to include two fifths or a little more of the circumference of the cornea. Only a small conjunctival flap is made. A suture of black silk is inserted in the conjunctival flap at 12 o'clock and placed aside to allow delivery of the lens. By means of a small toothed forceps the upper border of the wound is held open, and with the de Wecker scissors a small cut 1 or 2 mm. long is made horizontal in the root of the iris. When the combined method is adopted, the iridectomy is made before the conjunctival suture is placed.

The eye is then ready for the most important and the most talked of stage of the operation. Professor Elschnig uses his model of the capsule forceps. The capsule is grasped in the lower third by opening the forceps 2 or 3 mm. Gentle side-to-side motion is made five or six times, and pressure is made below at the limbus with the end of the strabismus hook. The capsule forceps are lifted toward the cornea and then up, breaking the zonula from below upward. Thus, the lens tumbles as it passes through the pupil, and the lower pole is the first part of the lens to be delivered through the incision. Follow the lens by pressure with the strabismus hook. Capsule forceps continue to hold the capsule until the lens is delivered.

Immediately after the delivery of the lens the conjunctival suture is tied, and the iris is carefully smoothed in place. Physostigmine (eserine), 1 per cent, is instilled; the bridle suture is cut; the wound is touched with iodine, 5 per cent, and oxycyanide ointment, 1 : 5,000, with 1 per cent physostigmine [1] is placed in the lower culdesac. The paralyzed

1. The formula is as follows: physostigmine salicylate, 0.1 Gm.; mercuric oxycyanide, 0.002 Gm.; hydrous wool fat, 6 Gm., and liquid petrolatum, 4 fluidrachms (15 cc.).

upper lid is carefully drawn down and covered with a square, thin piece of gauze well saturated with oxycyanide of mercury, 1 : 10,000.

Both eyes are bandaged for twenty-four hours, a perforated nickel-plated shield being placed over the eye operated on. Ordinarily the patient is in bed for one day. After five days the eye operated on is left open. The patients are usually sent home on the tenth day when one eye is operated on, and on the fourteenth day when both are operated on.

The treatment of iris prolapse depends on whether the prolapse is subconjunctival or free. A free prolapse is treated for two or three days with physostigmine, 1 per cent, and as soon as the eye becomes a little more quiet the prolapse is excised.

The prolapse below the conjunctiva is also treated for a few days with physostigmine until the conjunctival wound is healed. On the fourth or fifth day the eye is cocainized, and a retrobulbar injection of procaine hydrochloride is given. The conjunctival wound is then opened in its outer corner by a spatula, which is gently inserted between the conjunctiva and the prolapse. Thus, without opening the wound, the prolapse is reposed into the anterior chamber. This is always possible if there is no vitreous body under the prolapse. If there is a vitreous body, the prolapse must be excised.

INDICATIONS FOR SIMPLE AND COMBINED EXTRACTION

It is advantageous to get a round pupil in as many cases as possible, and, as is seen from the figures, in 247 cases, a round pupil resulted in 60 per cent. The percentage in the noncomplicated cases was 70.

Iridectomy was always performed on persons over 75 years of age and on obese persons, as well as on those with emphysema, on chronic coughers, on any patient with a complicating disease that did not favor smooth convalescence, on patients in whom the pupil dilated little or not at all with homatropine, 1 per cent, and on nervous or uncooperative patients.

The following is a report of 247 operations done consecutively over a period of six months.

Of this group, 206 were done intracapsularly by the method of Knapp-Török-Elschnig (K.T.E.). I shall mark the results of delivery according to the Elschnig method: The plus sign (+) designates the cases in which the lens was delivered in the intact capsule; the plus-minus sign (±), those cases in which the capsule ruptured during delivery, and the minus sign (—), the cases in which the capsule ruptured on being grasped by the forceps, or could not be grasped at all.

SIMPLE EXTRACTION

Simple extraction in the capsule was done in 129 uncomplicated cases as follows:

Female patients, 74
Male patients, 56

Age groups:

Years	Cases
80-90	2
70-80	19
60-70	72
50-60	19
40-50	13
30-40	4

	Kind and stage of cataract:	+	±	—
12	incipient	11	..	1
7	intumescent	2	3	2
21	immature	11	5	5
40	mature	31	4	5
8	hypermature	4	1	3
0	morgagnian	..	..	..
36	cortical	30	3	3
5	myopia (normal lens)	4	..	1
129		93 (72%)	16 (12.5%)	20 (15.5%)

Immature cataracts included those with slight involvement of the cortex and nucleus but no swelling of the lens.

The complications and results were as follows:

1. Vitreous loss: 1.
2. Vitreous in the anterior chamber: 0.
3. Reopening of the wound: 3 cases; all of the patients had iris prolapse: 2 were recorded as + and 1—. The percentage was 2.3.
4. Pupil central: 109; of which 84 were +; 12 ±, and 13, —; the percentage was 84.5.
5. Pupil eccentric: 20; 9 of which were +; 4, ±, and 7 —; the percentage was 15.5. Eccentric pupil included all degrees from slightly oval to the typical coloboma-like pupil in iris prolapse.
6. Vision calculated within one month after extraction:
   6/6-6/24, 120 cases.
   6/36-6/60, 5 cases.
   Less than 6/60, 4 cases; 3 of the patients had central choroiditis, and 1 macular degeneration in myopia.
7. Cases to be corrected by discission: 0.
8. Total loss: 0.

Of the 5 patients operated on for high myopia with a normal lens, all had vision between 6/6 and 6/24. In 4 the results were recorded as + and in 1 as —. The ages were 30, 33, 39, 42 and 43, respectively.

The percentage of vitreous loss in patients with a round pupil was 0.75.

Nineteen of the foregoing patients had high myopia with cataract. Of this number, the results in 15 were recorded as +; in 1 as ±, and in 3 as —.

The vision in these 19 patients was as follows:

6/6-6/24, 16.
6/36-6/60, 3.
Less than 6/60, 0.

The vitreous loss was in an apparently normal eye. The resulting vision was 6/12.

COMBINED EXTRACTION

Combined extraction in the capsule was performed in 54 uncomplicated cases, with the following results:

Female patients, 20
Male patients, 34

Age groups:

Years	Cases
80-90	4
70-80	26
60-70	15
50-60	8
40-50	1

	Kind and stage of cataract:	+	±	—
7	incipient	6	..	1
8	intumescent	6	2	..
9	immature	5	3	1
21	mature	13	3	5
2	hypermature	1	1	..
0	morgagnian	..	..	..
7	cortical	6	..	1
0	myopia (normal lens)	..	..	..
54		37 (68.5%)	9 (16.6%)	8 (14.8%)

The complications and results were as follows:

1. Vitreous loss: 3.
2. Vitreous in the anterior chamber: 0.
3. Reopening of the wound: 0.
4. Iris prolapse: 0.
5. Coloboma in order: 50, or 92.6 per cent.
6. Coloboma decentered: 3, or 7.4 per cent.
   This included the cases in which the lower pupillary border was distinctly elevated.

7. Vision within one month after extraction:
   6/6-6/24, 42 cases.
   6/36-6/60 6 cases.
   Less than 6/60, 3 cases; all of the patients had choroiditis.
   Candle at 6 meters, 1 case, in a mentally defective patient who was unable to cooperate.
8. Cases to be corrected by discission: 1.
9. Total loss (expulsive hemorrhage): 1.

In a few of the intumescent cataracts the anterior chamber was not opened by the Graefe knife, but with a scalpel from without in.

Nine of the foregoing cases were of high myopia with cataract. Of these, the results in 6 were recorded as +; in 2 as ±, and in 1 as —.

In the cases of vitreous loss, 2 patients had high myopia and 1 had an apparently normal eye.

Vision in the cases of myopia was as follows:

6/6-6/24, 7.
Less than 6/60, 2.

The higher percentage of vitreous loss in the combined method was caused by the fact that iridectomy was chosen for pathologic eyes in which one might expect vitreous and for patients who were naturally a greater operative risk. The percentage for combined extraction was 5.5.

SMITH METHOD

Eight patients with morgagnian cataract were operated on by the Smith method. Morgagnian cataracts are especially suited to this method, owing to the weak zonular fibers, and are poor for intracapsular forceps, owing to the impossibility of grasping the capsule.

Four patients were operated on by the simple method (round pupil), and the results in all of the cases were recorded as +.

Four patients were operated on by the combined method, and the results in 3 cases were recorded as +, and those in 1 case as —.

Vitreous was lost in the case in which the results were recorded as — and in which the combined method was used.

COMPLICATED CATARACT

Extraction was performed on 41 patients with complicated cataract. The causes for the complicated cataracts were as follows:

Trauma	11 cases
Cyclitis	17 cases
Glaucoma	5 cases
Syphilis	3 cases
Luxation	2 cases
Heterochromia	2 cases
Retinitis pigmentosa	1 case

The following procedures were carried out:

Simple extraction of complicated cataract (10 cases):

1. Intracapsular extraction
   - (a) + ... 3
   - (b) — 6
   - Total 9
2. Capsulotomy 1

Combined extraction of complicated cataract (31 cases):

1. Intracapsular extraction
   - \+ 11
   - ± 2
   - — 1
   - Total 14
2. Capsulotomy 16
3. Smith method 1

Vision in the 41 complicated cataracts:	Intracapsular Extraction	Smith Method	Capsulotomy
6/6-6/24	8	..	5
6/36-6/60	10	..	5
Less than 6/60	5	1	4
Candle at 6 meters	..	..	3
	23	1	17

Two patients with uncomplicated cases were operated on by the capsulotomy method. One patient had a round pupil, and the other one had a coloboma.

Thirteen patients were operated on by clinical assistants, and all of the results were satisfactory.

Summarizing, the complications were as follows:

1. Vitreous loss: 4 cases, or 2.16 per cent. This is the percentage of 183 uncomplicated cases in which the patients were operated on by the intracapsular method.
2. Iris prolapse: in 3 of 183 cases, or 1.6 per cent.
3. No cases of iritis.
4. No cases of infection.
5. Only 1 case to be corrected by discission, and in this case the results were recorded as —, 0.53 per cent.

Naturally, the foregoing report on 183 patients with uncomplicated cases recently operated on by the intracapsular method does not allow a report on what the condition of the eyes will be several years from now. In order to throw light on late results after successfully performed intracapsular operations, I have examined the charts of 848 cases seen during 1929, 1930 and 1931.

Every one realizes how difficult it is to follow up statistics, but the German Eye Clinic in Prague is fortunate to be so situated that practically all patients return if there is any reason for them to do so.

Only the cases in which the results were recorded as + and ± were considered, because in the cases in which the results were — the operator had the desire only to perform the intracapsular operation; that is, he was not successful in grasping the capsule or it tore on grasping, and he was forced to proceed extracapsularly.

REPORT OF CASES

Three cases of detachment of the retina were found.

CASE 1.—Ernst F., aged 65, had had high myopia since childhood. At the time of examination he was being treated for diabetes. On Oct. 29, 1930, the right eye was operated on intracapsularly; the result was recorded as +. The result was a round, central pupil; vision was 6/12 with + 3.00 sph. + 4.00 cyl., axis 180. At the end of three weeks the patient returned with severe iritis caused by a piece of thread from a sponge which had stayed in the wound. The thread had caused irritation and also fistulation. Three weeks later the patient returned to the clinic with a detached retina. Vision was limited to the perception of fingers at 3 meters. The patient did not decide on operation.

CASE 2.—Henrich L., aged 71, had myopia of 8 diopters. He was operated on on Oct. 23, 1928, by the intracapsular method; the result was recorded as +. Vision was 6/8 with + 5.00 + 4.00 cyl. He returned to the clinic one and one-half years later with detachment. He was operated on by ignipuncture, with no improvement. One year later vision was limited to light perception.

CASE 3.—Aloise K., aged 61, had myopia gravis. The right eye was operated on on Nov. 23, 1929, by the intracapsular method; the result was recorded as +. The pupil was central; vision was 2/24, owing to central choroiditis. The patient returned to the clinic on Oct. 5, 1931, with detachment; she was operated on by the Gonin method, with no improvement.

Two cases of glaucoma were seen.

CASE 4.—The left eye of Josephine S., aged 68, was operated on on March 14, 1929, according to the Stanculeanu-Török (St.T.) method. The result was recorded as ±. She returned to the clinic after six months with a slight increase in tension. She returned one and one-half years later, not having used the medicine ordered. There were a glaucomatous excavation and a small eccentric visual field. She again neglected treatment, and returned to the clinic in one year with vision limited to light perception in the left eye.

CASE 5.—Johann H., aged 49, had had myopia since childhood. Vision was 6/24 with — 20.00. He was operated on on Feb. 17, 1931, according to the K.T.E. method. The result was recorded as ±. Vision in the right eye was 6/8. The patient returned to the clinic in four weeks with glaucoma. Eight years before examination the left eye had become totally blind from unrecognized glaucoma after a combined extracapsular extraction. All this time the patient had been under a physician's care.

Two cases of iridocyclitis are recorded.

CASE 6.—Marie D., aged 78, was operated on on March 31, 1930, according to the K.T.E. technic; the result was recorded as ±. There was a coloboma in order; vision was 6/36. The patient returned to the clinic six months later with severe iridocyclitis which did not yield to treatment. The eye was enucleated on Jan. 2, 1931.

CASE 7.—Thomas J., aged 56, was operated on on Sept. 18, 1928, according to the K.T.E. technic; the result was recorded as +. He had a round pupil; vision was 6/60. He returned to the clinic on June 14, 1931, and the eye was amaurotic and painful and had to be enucleated. The patient stated that the eye became inflamed one year after operation and continually became worse.

One case of late iris prolapse was seen.

CASE 8.—Alois W., aged 59, was operated on on Jan. 7, 1931, according to the K.T.E. method; the result was recorded as +. He had a round central pupil; vision was 6/8. He returned to the clinic six weeks later with iris prolapse; vision was 6/12. Iridectomy was performed, and vision was lowered to 6/60 on November 3. The patient was not seen later.

Four patients were found with late drawn-up pupils.

Three patients were discharged with round central pupils and returned within from six to eight weeks with high coloboma-like pupils. The fourth patient had a combined extraction and returned six months later with a high pupil.

The number of late complications in 848 cases were as follows:

1. Retinal detachment	3
2. Glaucoma	2
3. Iridocyclitis	2
4. Iris prolapse	1
5. Drawn-up pupil	4

The least serious of the complications is the drawn-up pupil, which has a marked cosmetic result and at times a visual effect. The cause seems to be one of two things: (1) the attachment of zonular fibers to the posterior surface of the iris and later shrinkage of the fibers along with the ciliary body; (2) a hammock caused by vitreous threads through the pupil and into the wound with later shrinkage.

COMMENT

Several of the foregoing cases are reported and discussed in Professor Elschnig's recently published book on intracapsular extraction.[2] The book covers the various methods of intracapsular extraction along with many important suggestions, statistics and references. The publication is in German, and it is hoped that its field will be increased by an English translation.

2. Elschnig, Anton: Die intrakapsulare Starextraktion, in Saemisch, T.: Handbuch der gesamten Augenheilkunde, ed. 2-3, Berlin, Julius Springer, 1932.

UVEAL PIGMENT

HYPERSENSITIVITY AND THERAPEUSIS

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In 1925, one of us (Dr. Woods [1]) reported a summary of experimental work previously done in the investigation of Elschnig's allergic theory of sympathetic ophthalmia and the occurrence of a hypersensitivity to uveal pigment which commonly appeared in this disease. The results of treatment with pigment, the principle of which was desensitization with an organ-specific ocular substance in patients in whom a specific hypersensitivity had been demonstrated, were likewise reported. At this time the opinion was expressed that, while there was an apparently definite allergic phase to sympathetic ophthalmia, yet this did not appear to be the only phase of the disease, and it was quite probable that other factors entered into the problem.

Since the publication of this report, other authors have reported on the allergic phase of sympathetic ophthalmia; much other interesting experimental work has been done, and our own experience with pigment hypersensitivity has been considerably enlarged. Before reporting our further clinical studies on pigment hypersensitivity, it is well to review the work of others on this special manifestation of the disease and to summarize the present conflicting views on the pathogenesis of sympathetic ophthalmia.

REVIEW OF THE RECENT LITERATURE

Fodor [2] repeated our earlier work on the appearance of complement-binding antibodies in the blood serum following injuries to the uveal tract. While he demonstrated the presence of such antibodies in many cases, he did not agree with us as to their occurrence in specific conditions. Thus he found them only irregularly in eyes that healed uneventfully, while in our experience their occurrence in such conditions was

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1. Woods, Alan C.: Sympathetic Ophthalmia: The Use of Uveal Pigment in Diagnosis and Treatment, Tr. Ophth. Soc. U. Kingdom **45**:208, 1925.

2. Fodor, G. I.: Komplementbindungsreaktion mit Pigment bei Augenverletzungen, Klin. Monatsbl. f. Augenh. **79**:759 (Dec. 30) 1927.

practically constant. He agreed with us in their absence in sympathetic ophthalmia. He found such antibodies irregularly in pigmentary degeneration of the retina and in other diseases of the uveal tract.

Gifford [3] failed to find complement-binding antibodies to pigment in four cases of penetrating wounds of the uveal tract, in two of which sympathetic ophthalmia developed. He found the intracutaneous test with pigment negative in two cases of sympathetic disease and in two cases of penetrating wounds of the eye without sympathetic disease.

Verhoeff [4] likewise found the intracutaneous test negative in one case of clearcut sympathetic ophthalmia. Berens [5] reported eighteen cases in which intracutaneous tests with pigment were made, all of which were negative, and in no case did sympathetic ophthalmia develop. On the other hand, Gill [6] found the intracutaneous test with pigment positive in sympathetic disease and negative in other conditions, and believed that clinical improvement, at times spectacular, followed the use of uveal pigment as a therapeutic agent in sympathetic ophthalmia, especially when used early.

The similarity of the pathologic picture in sympathetic ophthalmia to certain tuberculous lesions of the uveal tract has long been recognized, and Guillery [7] has endeavored to demonstrate by experimental procedures that sympathetic ophthalmia is in its essence a tuberculotoxic disease. Guillery inserted semipermeable capsules containing living tubercle bacilli in pouches between the ciliary body and the sclera of the eyes of rabbits and later directly into the vitreous chamber of rabbits' eyes. The tuberculous toxin diffusing out from these capsules produced disease first in the inoculated eye and later in the fellow eye. Guillery believed that these lesions were identical with those of sympathetic ophthalmia. On the basis of these experiments, he expressed the view that sympathetic ophthalmia is tuberculotoxic in origin. This view was partially endorsed by Kolen,[8] who repeated the experiments with tubercle

3. Gifford, S. R.: Modern Views of Sympathetic Ophthalmia, Nebraska M. J. **14**:432 (Nov.) 1929.

4. Verhoeff, F. H.: Effective Treatment for Sympathetic Uveitis, Tr. Am. Ophth. Soc., 1926, p. 173; Arch. Ophth. **56**:28 (Jan.) 1927.

5. Berens, Conrad, and others: Studies in Immunology in Relation to Ophthalmology, Atlantic M. J. **30**:547 (June) 1927.

6. Gill, W. D.: Uveal Pigment in the Diagnosis and Treatment of Sympathetic Ophthalmia, South. M. J. **23**:885 (Oct.) 1930.

7. Guillery, H.: Die sympathische Ophthalmie, eine tuberkulotoxische Erkrankung, München. med. Wchnschr. **72**:298 (Feb. 20) 1925; Experimentelle Sympathisierung des Kaninchenauges, Arch. f. Augenh. **94**:143, 1925; Experimentelle sympathische Ophthalmie bei extrabulbärem tuberkulösem Herd, Klin. Monatsbl. f. Augenh. **76**:567, 1926; Klinisches und Histologisches zur Sympathisierung des Kaninchenauges, Arch. f. Augenh. **99**:63 (May) 1928.

8. Kolen, A.: Ueber die Wirkung der Toxine des Staphylococcus aureus und des Tuberkelbacillus auf den Uvealtraktus (zur Pathogenese der sympathischen Ophthalmie), Russk. Oft. **8**:320, 1928.

bacilli and obtained similar results, but with capsules containing staphylococci he obtained negative results. He did not believe that the lesions produced in the inoculated eye were entirely characteristic of sympathetic ophthalmia, but that the proliferative choroiditis produced in the second eye was identical with the early stage of sympathetic disease. On the other hand, Meesmann and Volmer,[9] inquiring into the cause of sympathetic ophthalmia, greatly doubted Guillery's conclusions, and Poos and Sartorius,[10] while confirming Guillery's experimental work, reached radically different conclusions. These authors believed that the picture produced in the experimental eyes was a toxic endophthalmitis in which no initial injury was necessary to the first eye, and that the lesions produced in the eyes were the result of general toxic injury to the entire reticulo-endothelial system and had nothing to do with the process in human sympathetic ophthalmia. Marchesani[11] likewise criticized Guillery's views, believing that the tubercle-like structures seen in sympathetic ophthalmia occur in many chronic inflammatory reactions due to toxins, and are the expression of an immune-biologic defense mechanism of the body. He called attention to the fact that the capsules used by Guillery could not be made entirely impermeable to tubercle bacilli, and he sharply disagreed with Guillery's assumption that sympathetic ophthalmia is a tuberculotoxic disease.

The most interesting of the recent contributions on the pathogenesis of sympathetic ophthalmia are the experiments with filtrable viruses. Von Szily[12] was the first to investigate this question. In 1924, he reported a series of experiments. The material from a herpetic lesion on the human cornea was injected into rabbits' eyes. After the characteristic herpetic keratitis had developed, the superficial layers of the cornea were removed, and this material was inserted in ciliary pouches of the eyes of other animals. In these animals uveitis of the eye followed injection, and in 10 per cent a similar uveitis developed in the second eye. The papilla and optic nerve showed similar infiltration with lymphocytes and epithelioid cells. Going on the theory that filtrable viruses have a predilection for nerve tissue, he believed that the

9. Meesmann, A., and Volmer, W.: Zur Frage nach der Ursache der sympathischen Ophthalmie, Arch. f. Augenh. **98**:271 (Sept.) 1927.

10. Poos, F., and Sartorius, F.: Experimentelle Untersuchungen zur Frage einer tuberkulotoxischen Genese der sympathischen Ophthalmie (Guillery), Arch. f. Ophth. **124**:565, 1930.

11. Marchesani, O.: Ueber die Beziehungen der sympathischen Ophthalmie zur Tuberculose, Klin. Monatsbl. f. Augenh. **81**:868, 1928.

12. von Szily, A.: Experimentelle Endogene Infektionsübertragung von Bulbus zu Bulbus: Ein Beitrag zur Erforschung der sympathischen Ophthalmie und zur Pathogenese des hämatogenen herpes corneae, Klin. Monatsbl. f. Augenh. **72**:593, 1924.

mode of transmission from eye to eye was by way of the optic nerve. This work was confirmed by Abe,[13] by Velhagen [14] and by Gifford and Lucic [15] in this country. Gifford and Lucic [16] further extended these observations by showing that herpetic virus inoculated as far back as the chiasm in the eyes of experimental rabbits produced lesions that spread forward along the nerves and produced uveal disturbances in both eyes. Marchesani,[17] however, repeated the experiments of von Szily with negative results.

On the supposition that sympathetic ophthalmia might be due to an ultramicroscopic, uncultivable virus contained in the tissues of the eye, numerous observers have attempted to produce the disease in the eyes of rabbits by the direct inoculation of material from active human sympathetic disease into the eyes. In 1927, Gifford and Lucic [15] inoculated ten rabbits with the contents of a sympathetic eye with entirely negative results, except in one instance. In this, they offered the explanation that secondary contamination might be responsible. Meesmann and Volmer,[9] using material from five cases of sympathetic ophthalmia, inoculated sixty rabbits by the ciliary pouch method. Material from one case produced a uveitis in the second eye of three rabbits. Two of these animals on postmortem examination were found to have tuberculosis, but the third showed no lesions at autopsy. They believed, however, that there was a possibility that the disease in the eye of the last rabbit was due to herpetic virus acquired as a stall infection. Lešer,[18] Marchesani [19] and Undelt [20] did somewhat similar experiments,

13. Abe, T.: Experimente über die durch Herpesvirus erzeugte sympathischen Ophthalmie (v. Szily) unter besonderer Berücksichtigung der Fortleitungsbahn, Arch. f. Ophth. **117**:375, 1926.

14. Velhagen, K., Jr.: Experimente mit Herpesvirus zur Frage der Infektionsübertragung von Bulbus zu Bulbus, Arch. f. Ophth. **119**:325, 1928; Experimentelle Untersuchungen über die Beteiligung des Sehnerven bei Entzündungen des vorderen Bulbusabschnittes, Klin. Wchnschr. **6**:828, 1927.

15. Gifford, S. R., and Lucic, L. H.: Sympathetic Uveitis Caused by Virus of Herpes Simplex: Experiments, J. A. M. A. **88**:465 (Feb. 12) 1927.

16. Gifford, S. R., and Lucic, L. H.: Etiology of Sympathetic Ophthalmia: Further Notes, Arch. Ophth. **1**:468 (April) 1929.

17. Marchesani, O.: Weitere Beiträge zur Frage der Beziehungen des Herpesvirus zur sympathischen Ophthalmie, Arch. f. Augenh. **97**:575 (Dec.) 1926.

18. Lešer, O.: Zur Ätiologie der sympathischen Ophthalmie, Časop. lék. česk. **67**:934 (June 22) 1928.

19. Marchesani, O.: Neues zur sympathischen Ophthalmie mit besonderer Berücksichtigung der Bedeutung des Herpesvirus, Klin. Monatsbl. f. Augenh. **75**: 218, 1925.

20. Undelt, J.: Ein Fall von Heilung einer sympathischen Ophthalmie nach interkurrentem Scharlach, mit experimentellen Beiträgen zur Beziehung des Herpesvirus zur sympathischen Ophthalmie, Klin. Monatsbl. f. Augenh. **76**:825, 1926.

again with entirely negative results. In a criticism of this work, the attractiveness of a filtrable agent as the responsible etiologic factor in sympathetic ophthalmia cannot be denied, and the negative results of animal inoculation, while disappointing, are certainly inconclusive. One of us (Dr. Woods) has been greatly struck by the similarity, both in the clinical and in the pathologic picture, of periodic ophthalmia in horses and sympathetic disease in man. The essential clinical pictures are almost identical, and there is some resemblance in the pathologic pictures. In equine periodic ophthalmia the demonstration that the disease is due to a filtrable virus appears to be conclusive.[21] Further, it must be remembered that not all species of animals are susceptible to the various filtrable viruses and that in susceptible species a certain number of individuals appear to be naturally immune. For this reason the negative inoculation experiments are inconclusive.

Meanwhile, a third school of thought as to the pathology of sympathetic ophthalmia appears to have been developing. This is in line with the suggestion advanced by us in 1925, that allergy, plus some other existing agent, might produce the characteristic picture of the disease. This view was again expressed by Key[22] in 1926, that a developing pigment hypersensitivity predisposes the second eye to other noxious agents and determines the characteristic clinical course. In 1930, Marchesani[23] reported an interesting experiment. He isolated Bacillus subtilis by the antiformin method from the enucleated exciting eye in a case of sympathetic ophthalmia. Repeated injections of this bacillus into one eye of rabbits finally produced a choroiditis in the untouched eye. No changes were noted in the other tissues. After the acute inflammation subsided the pathologic picture was found to be round cell infiltration of the uvea of the inoculated eye and lymphocytic infiltration only in the choroid of the sympathizing eye. Judging from the anatomic changes along the nerves, the transmission did not occur by the nerve pathway. Marchesani believed that this was not a question of simple metastases, but that the changes in the second eye were due to developing allergy to this specific bacillus, which makes its localization in the second eye possible. In short, a paired organ sensitivity developed, which explained the localization of the exciting organism in the fellow eye, while it was not found in other parts of the body. This work was

21. Woods, Alan C., and Chesney, Alan M.: The Transmission of Periodic Ophthalmia of Horses by Means of a Filterable Agent, J. Exper. Med. **52**:637 (Oct.) 1930.

22. Key, B. W.: Sympathetic Ophthalmia Cured After Exenteration of Nasal Accessory Sinuses, Am. J. Ophth. **9**:574 (Aug.) 1926.

23. Marchesani, O.: Zur Pathogenese der sympathischen Ophthalmie, Zentralbl. f. d. ges. Ophth. **22**:804, 1930.

repeated, however, by Iga,[24] who sharply criticized Marchesani's views; he believed that bacterial metastases in the second eye were responsible for the picture, and he further emphasized the fact that Bacillus subtilis was by no means nonpathogenic for rabbits. It must be remembered in this conclusion that it had already been demonstrated by Guillery,[25] and later by one of us, that such ferment-producing organisms as Bacillus subtilis may produce protein degeneration products in the mediums in which they are grown, which have a specific irritative effect on the ciliary body. Riehm,[26] however, after a series of interesting experiments modeled along the earlier experiments of Wessely, reached the conclusion that a foreign protein absorbed from one eye produced an elective sensitivity in the fellow eye. This was true only in pigmented rabbits. In albinotic rabbits no such elective sensitivity of the paired organ was produced. He believed that similar organs with a common trophonervous influence were a closed entity and had a common inflammatory reaction, which should be designated as elective sensitization rather than as a sympathetic disease. In sympathetic ophthalmia he believed that one might be dealing with different etiologic conditions. In penetrating wounds he said that one was dealing with infection produced by an agent that possesses specific affinity for uveal tissue, which sensitizes the uvea of both eyes. In sympathetic ophthalmia such as might follow disintegrating choroidal sarcoma or subconjunctival scleral rupture, inflammation of the uvea of both eyes might be regarded as a purely allergic process, the involvement of the second eye being due to the phenomenon of elective sensitization. On the basis of his experiments and argument, he further expressed the belief that the action of tuberculin and tuberculous toxin might be similarly explained on such a doctrine of anaphylaxis. Various other authors, without reporting experimental work, have emphasized the idea that the outbreak of sympathetic ophthalmia in the second eye may be due to a modification of the uvea of the second eye through allergy or endogenous infection, which renders it liable to the action of other noxious agents.

The three chief views on the etiology of sympathetic ophthalmia which have developed in the last six years may be summarized as

24. Iga, F.: Zur Frage der Sensibilisierung und der „Sympathischen Choroiditis" mit Bac. subtilis, Klin. Monatsbl. f. Augenh. **83**:195 (Aug.-Sept.) 1929.

25. Guillery, H.: Untersuchungen über Uveagifte, Arch. f. Augenh. **78**:2, 1914.

26. Riehm, W.: Zur Frage der anaphylaktischen Iritis, Klin. Monatsbl. f. Augenh. **81**:867, 1928; Experimentelle Uebertragung eines lokalen Ueberempfindlichkeitszunstandes von einem paarig angelegten Organ auf das andere, zugleich ein Beitrag zur Genese der sympathischen Ophthalmie, Deutsche med. Wchnschr. **55**:907 (May 31) 1929 (comment by Marchesani, p. 1133; reply by Riehm, p. 1134); Ueber die Bedeutung der Anaphylaxie für den klinischen Ablauf der sympathischen Ophthalmie, der Tuberkulose und der Organgebundenen-infektionskrankheiten, Arch. f. Ophth. **123**:361, 1930.

follows: 1. The idea that sympathetic ophthalmia is a tuberculotoxic disease, the experimental work in favor of which is far from convincing and for which confirmation is lacking. 2. The extremely attractive and stimulating idea that sympathetic ophthalmia is in its essence a disease due to a filtrable virus, a theory that has much to commend it, but for which no specific proof has as yet been brought forward. 3. The idea that the disease may be due to a filtrable virus or to other forms of noxious agents, but in order for the disease to develop in the second eye, there must be an allergic factor, a developing sensitivity in the fellow eye, which makes it especially susceptible to the influence of other exciting agents.

It is the purpose of this paper to report an analysis of our further clinical experience with pigment hypersensitivity over the past six years,

Results of Intracutaneous Pigment Test in One Hundred and Fifty-Three Patients

	Intradermal Pigment Test	
	Positive	Negative
Uveitis due to constitutional causes	0	27
Contusions with traumatic uveitis; no sympathetic disturbance	0	11
Operation involving uveal tract; uneventful recovery	0	8
Operation involving uveal tract; eyes lost; no sympathetic disturbance	0	11
Endophthalmitis phaco-anaphylactica	1	3
Penetrating wound involving uveal tract; recovery without enucleation; no sympathetic ophthalmia	3	38
Penetrating wounds involving uveal tract; enucleation of injured eye; no sympathetic ophthalmia	5	21
Delayed, noninfectious, postoperative uveitis	5	0
Sympathetic ophthalmia	18	2
Total	32	121

and to endeavor to determine what rôle, if any, hypersensitivity to uveal pigment may play in uveal inflammation and sympathetic ophthalmia. Since our last report was published in 1925, one hundred and fifty-three intracutaneous tests with uveal pigment have been done in the Wilmer Institute on patients with a variety of ocular conditions. The technic of the test is essentially the same as before reported, the only change being that after the pigment is prepared it is weighed and solutions of standard strength are prepared. Three definite solutions are made—a 0.5 per cent solution which is diluted 1 : 10, and then 1 : 20—and 0.1 cc. of each of these solutions is injected into the skin of the forearm about 5 cm. apart. As a control either beef aqueous or beef serum, containing the same proportion of cresol (tricresol solution) used to preserve the pigment—0.25 per cent—is employed. The tests are read at the end of twelve, twenty-four, thirty-six and forty-eight hours. Positive tests are usually observed at the end of twenty-four hours, and usually disappear at the end of from forty-eight to seventy-two hours. Great care is needed in the reading of these tests. Sometimes they are strongly posi-

tive and can be detected at once. Occasionally very slight reactions only are seen around the site of injection of the strongest dilution. The exact nature of this reaction will be discussed later.

The results of the intracutaneous pigment test in the patients on whom this study is based are shown in the accompanying table. Thirty-two of these tests gave positive results, while one hundred and twenty-one gave negative results. It is necessary to analyze the various pathologic conditions into which the cases of these patients naturally fall before any realization of the significance of the positive pigment test can be reached.

PATHOLOGIC CONDITIONS IN CASES STUDIED

GROUP I.—*Uveitis Due to Constitutional Causes; No History of Injury.*—There were twenty-seven patients in this group, who suffered from prolonged chronic uveitis. These patients were subjected to a complete medical survey, and in each instance the disease was believed to be due to some constitutional cause, such as syphilis, tuberculosis or focal infection. The patients were all given intracutaneous tests with pigment, and in all instances the test was entirely negative.

GROUP II.—*Nonpenetrating Wounds of the Eye; Traumatic Uveitis; No Sympathetic Disturbance.*—There were eleven patients in this group. Each of the patients had suffered from contusion of the eyeball, resulting in traumatic uveitis of greater or lesser intensity. In no case was there a penetrating wound of the eye, and likewise no development of sympathetic disturbance in the fellow eye. In each of the eleven patients an intracutaneous test with uveal pigment was negative.

GROUP III.—*Operation Involving the Uveal Tract; Uneventful Recovery.*—The eight patients in this group were given intracutaneous pigment tests. They were all either patients with cataract or patients on whom an iridectomy had been done for one cause or another. All of the patients had an uneventful postoperative course with no complications of any type. In all of these patients the intracutaneous tests were negative.

GROUP IV.—*Operation Involving the Uveal Tract; Eyes Operated on Lost Through Postoperative Infection; No Sympathetic Disturbance.*—The eleven cases in this group were in patients whose eyes were lost following the extraction of a cataract or some other intra-ocular operation involving an iridectomy. Postoperative infection and uveitis developed, with loss of the eye on which operation was performed. In no case was there any sympathetic disturbance. The intracutaneous pigment test on all the patients was negative.

GROUP V.—*Endophthalmitis Phaco-Anaphylactica.*—There were four patients in this group. Three of the patients showed a prolonged,

apparently nonseptic, uveal inflammation following the extraction of a cataract, associated with the development of a definite hypersensitivity to lens protein. These three patients were treated by desensitization with lens protein, with more or less satisfactory results. In all of the patients the uveal pigment test was negative. The fourth patient in this group was most interesting. In a small child an unexplained uveitis of the right eye developed after a minor injury to the eye in which there was a question of a penetrating wound. Prolonged and careful diagnostic study failed to show any constitutional cause for the inflammation. Extensive pigmentary degeneration of the iris occurred, and finally phthisis developed. A uveal pigment test was faintly positive. A lens protein test was not done on this patient, for there was no suspicion of the condition shown by histologic examination. The phthisical eye was enucleated, and pathologic examination showed the picture of endophthalmitis phaco-anaphylactica, as described by Verhoeff, and no evidence of sympathetic disease. This case is grouped here on account of the pathologic diagnosis, although it may more properly belong with the five patients with positive intracutaneous tests in group VII.

GROUP VI.—*Penetrating Wounds of the Eye Involving the Uveal Tract; Recovery Without Enucleation or the Development of Sympathetic Disease.*—There were forty-one patients in this group. All of these patients went on to uneventful recovery after the penetrating wound, the end-picture being quiet eyes entirely free from inflammation, with a varying amount of vision remaining, according to the extent of the injury. In no case was there any evidence of sympathetic disease. Thirty-eight of these patients gave a negative intracutaneous test with pigment. Two patients gave a doubtful positive reaction to pigment around the strongest dilution only. One patient gave a strongly positive reaction to all dilutions of pigment. The histories of the three patients with positive reactions are as follows:

CASE 1.—The patient had a penetrating wound of the left eye with prolapse of the iris tissue. The prolapsed tissue was removed the following day, and the wound closed. The patient did badly for some time. Enucleation was advised but refused. The pigment test became faintly positive to the strongest dilution. The injured eye finally quieted. The patient was under observation for one year, during which time the injured eye remained quiet and there was no evidence of sympathetic disturbance in the other eye. No further information on this patient is available.

CASE 2.—The patient was a child, aged 8, who suffered from laceration of the left eyeball and incarceration of the prolapsed iris tissue at the limbus. Iridectomy and excision of the prolapsed iris tissue were done immediately following the injury. The eye quieted rapidly, and 20/30 vision resulted. Two weeks afterward there was a doubtfully positive reaction to pigment around the injection of the strongest dilution only. The child was discharged from the hospital. Efforts to obtain further information in this case have been unsuccessful.

In both of these patients the reactions were doubtfully positive, and they might possibly be classified as negative.

CASE 3.—A boy, aged 9, suffered from a penetrating corneal injury of the left eye with prolapsed iris tissue. Excision of the prolapsed iris and repair were done twenty-four hours after injury. The eye did remarkably well. Two weeks later the boy showed a strongly positive pigment test to all dilutions, which hypersensitivity has steadily persisted over a period of ten months. There has, however, been no evidence of inflammation in the injured eye, and likewise no evidence of sympathetic ophthalmia. This case will be referred to later.

GROUP VII.—*Penetrating Wounds of the Eye Involving the Uveal Tract; Injury and Clinical Course of the Case Necessitated Enucleation of the Injured Eye; No Pathologic or Clinical Evidence of Sympathetic Ophthalmia.*—There were twenty-six patients in this group. In all of these patients the injury and subsequent clinical course were so severe that the eyes were totally lost and enucleation was performed. In none of the cases did histologic examination of the enucleated eyes show any evidence of sympathetic ophthalmia. Twenty-one of the patients had negative intracutaneous tests with pigment.

There were five patients in this group, however, who gave positive pigment reactions. Four of the patients were in the wards of the Wilmer Institute and presented similar clinical pictures. The last patient was seen only after the injured eye had been enucleated, but appears to belong in this general group. Following is a clinical and pathologic summary of the cases of these five patients. The histologic reports are by Dr. Jonas Friedenwald.

CASE 1.—The right eye suffered a penetrating wound and resultant traumatic cataract. The eye was operated on, and the cataract was later extracted. The eye did extremely well for several weeks and then a low grade cyclitis developed. Three months after the injury the patient showed a positive uveal pigment test. The injured eye improved and a relapse then occurred, giving a final picture of an inflamed, painful eye with chronic iridocyclitis, but without evidence of infection. The eye was enucleated.

Histologic Examination: The eye showed an intense plastic iritis, the iris stroma being infiltrated with lymphocytes and plasma cells. No epithelioid cells were to be found in this eye.

CASE 2.—A child, aged 7, had bilateral buphthalmos and dislocated lenses. An iridectomy was performed, and the dislocated lens fell back into the vitreous. The child did well at first, and then the eye became chronically inflamed and finally phthisis occurred. The eye appeared clinically dangerous and was enucleated. The patient gave a positive uveal pigment test.

Histologic Examination: The eye showed a rather intense lymphocytic infiltration of all the ocular tissues. The anterior surface of the iris was plastered with large mononuclear wandering cells, and there was one giant cell in the iris stroma near the angle. The only other unusual feature in this case was an extensive proliferation of the retinal pigment epithelium, which formed a dense sheet attached to the undersurface of the detached retina (fig. 1).

CASE 3.—A boy, aged 17, suffered from a penetrating wound of the right eye caused by a shot. The shot was removed by a magnet the same day. The eye

Fig. 1.—Epithelioid and giant cells in the root of the iris.

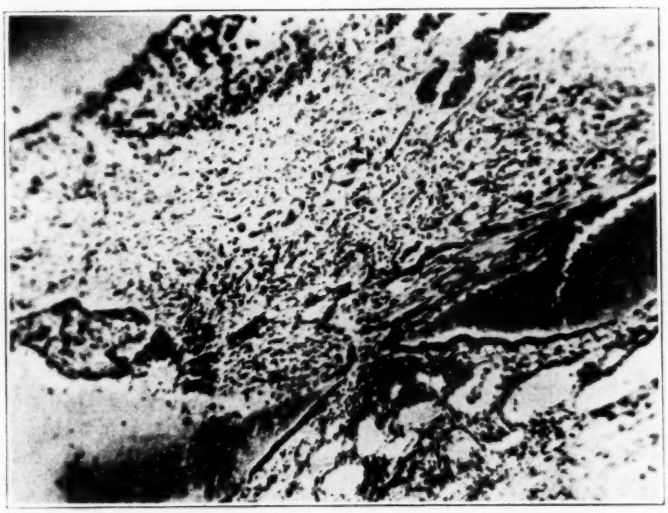

Fig. 2.—Proliferation of the pigment epithelium beneath the detached retina.

showed no evidence of infection, but later uveitis developed. Two weeks after the injury, a uveal pigment test was definitely positive. At this time there was a development of some photophobia in the fellow eye. The right eye was immediately enucleated. Sympathetic ophthalmia did not develop.

Histologic Examination: The eye showed old scars that contained a good deal of blood pigment, and were probably the result of the organization of old hemorrhages. The active infiltration in this eye, except in relation to the organizing hemorrhages, was very slight. There was, however, the same proliferation of the retinal pigment epithelium attached to the undersurface of the retina as seen in case 2 of this group (fig. 2).

CASE 4.—A child, aged 10, four months previous to admission had suffered from a penetrating wound of the eye caused by a butcher knife. On admission, the corneal wound was healed, but the iris was caught up in the corneal wound, the anterior chamber was abolished, there was a definite chronic cyclitis, and the eye

Fig. 3.—Epithelioid cells in the ciliary body.

was without light perception. The uveal pigment test at this time was definitely positive. The eye was enucleated.

Histologic Examination: The eye showed massive old scars and marked disorganization of the intra-ocular structures, but only very little active inflammatory reaction. The latter consisted of a scattering of round cells throughout the intra-ocular structures. There were, however, one focus of epithelioid cells surrounding the disintegrated pigment epithelium of a ciliary process (fig. 3) and proliferation of the pigment epithelium on the undersurface of the detached retina (figs. 4 and 5).

CASE 5.—This patient suffered from bilateral injury to the eyes caused by a dynamite cap explosion. The left eye showed prolonged inflammation and was enucleated at another hospital. After the right eye had quieted down, the patient was sent to the Wilmer Institute to have the traumatic cataract extracted. The uveal pigment test on this patient was likewise positive. There was no evidence of sympathetic ophthalmia. The cataract was extracted, with restoration of a moderate degree of vision. There was no pathologic specimen available in this last case.

Fig 4.—Proliferation of the pigment epithelium beneath the detached retina.

Fig. 5.—Proliferation of the pigment epithelium beneath the detached retina.

The first four patients of this group showed the common finding of a prolonged posttraumatic uveitis, the eyes going steadily downhill until, from their clinical appearance alone, enucleation was performed. None of them showed sympathetic ophthalmia, but all had a positive uveal pigment test.

The first of these cases showed only the picture of a general, nonspecific, noninfectious, posttraumatic iritis. The remaining three cases showed a histologic picture quite comparable with, but somewhat different from, the usual picture of nonspecific, noninfectious, traumatic uveitis. They showed definite proliferation of the retinal pigment epithelium, occasional foci of epithelioid cells and, in one case, a definite giant cell—a resemblance, though somewhat faint and remote, to the picture of sympathetic ophthalmia. Further study of the histologic picture of such eyes will be necessary before it can be determined whether or not this suggestive picture is a constant finding. The rather uniform clinical course of these patients, associated with a positive intracutaneous test to pigment, and the suggestive common pathologic findings shown in three of the four eyes examined indicate that there may be in such cases not only a concrete clinical entity, but what may also be a pathologic entity.

GROUP VIII.—*Delayed, Noninfectious, Postoperative Uveitis.*—This group of five patients is most interesting. Two of the patients have been carefully followed over a period of five years, and present a remarkable, almost identical clinical picture. The other three were only casually observed, but apparently belong to the same disease group entity. The characteristic finding in this group of five patients is the development of a delayed, noninfectious uveitis following an intra-ocular operation. All of the patients did well at first. Several weeks later a low grade uveitis developed in the eye operated on without any of the characteristic signs of ordinary infection. A most careful and painstaking medical survey failed to reveal any condition that could be regarded as a causal factor in the development of the uveitis. All of the patients gave a positive pigment test. In two patients the original operation had been performed in other clinics, and the patients presented themselves at the Wilmer Clinic when the uveitis was, respectively, of one and four years' duration. The only positive findings were the reactions to uveal pigment. These patients were not treated with pigment, but were discharged unimproved, and at the last reports they were still suffering from the same low grade uveitis, with gradual loss of vision. The third patient in this group was operated on in the Wilmer Institute in 1925; the patient did well for several months, and then a low grade uveitis developed for which no cause could be found. The patient showed a positive pigment test synchronous with the development of the uveitis. This

patient disappeared from observation, and we have no further information concerning the ultimate outcome. The two remaining patients in this group have been under observation for periods of five and six years, respectively. One of the patients, a man, aged 43, with bilateral posterior cortical cataracts, had a preliminary iridectomy, extraction of the left lense and later discission with uneventful results, 20/15 vision resulting. Two months after the discission he noticed a gradual failure of vision in the eye on which operation was performed. Examination showed the vision reduced to 20/70, definite veils in the anterior vitreous and a small central scotoma. A careful medical survey was essentially negative. The patient was found to be definitely hypersensitive to uveal pigment. In the absence of other positive findings, uveal pigment therapy was started with an initial dose of 0.5 cc., which was gradually increased to a maximum dose of 5 cc. Under this treatment the eye cleared steadily, the haziness of the anterior vitreous disappeared, and the central scotoma cleared. The vision again rose to 20/15. The dose of pigment was then reduced to 0.5 cc., given every five days, and this treatment was continued over a period of two years. At the end of this time the patient was found to be completely desensitized and pigment therapy was abandoned. There have been no further changes in the eye since that date. The eye is now free from inflammation, with 20/15 corrected vision.

The other patient was a white man, aged 63, who entered the Wilmer Institute with bilateral posterior cortical cataracts. A complete medical survey was made with entirely negative results. An intracutaneous test with lens protein, before operation, was likewise negative. A preliminary iridectomy and later extraction and discission were done on the right eye, the date of the discission being Feb. 25, 1926. Following these procedures the patient had 20/20 vision, which was maintained uneventfully for a period of about one month. At the end of this time a very low grade central chorioretinitis developed in the eye operated on, associated with a small central scotoma. This inflammation spread rapidly, and generalized uveitis developed, with heavy mutton fat deposits on the posterior surface of the cornea. Vision was reduced to 20/100. Again a complete and exhaustive medical survey was essentially negative. The patient was given all forms of local treatment and nonspecific therapy, but without effect on the ocular condition. In July, 1926, the tests with uveal pigment and lens protein were repeated. Both tests were found to be strongly positive. The patient was then given therapeutic injections of both lens protein and uveal pigment. Under this treatment the uveitis cleared steadily; vision in the right eye rose, until by November it was 20/20 +, with evidence only of the residua of a uveitis. Therapy with lens and pigment was discontinued on March

23, 1927, when intracutaneous tests with both pigment and lens were negative. The patient was not seen again until November, 1929, when he returned with vision reduced to 20/40 in this eye, and stated that the eye had been entirely quiet up to the summer of 1928, when low grade attacks of uveitis began to recur. There were several such attacks, culminating in a rather sharp attack in the fall of 1929. On examination, the patient showed definite low grade, chronic uveitis with minor changes in the foveal area of the right eye. Intracutaneous tests with lens protein and uveal pigment were both definitely positive. The patient was again given therapy with both uveal pigment and lens protein, which was continued up to Feb. 13, 1930, when all signs of uveal inflammation had disappeared. Combined extraction of the cataract in the left eye was done. This eye did well for two weeks, and then small posterior corneal deposits and other evidences of low grade uveitis developed. The injections of uveal pigment and lens protein were resumed, and the eye gradually cleared. The patient was finally discharged in the late spring of 1930, with both eyes quiet and free from inflammation, 20/50 vision remaining in the right eye and 20/15 in the left eye. He was tested for the recurrence of hypersensitivity to both lens protein and uveal pigment in the fall of 1930, and again in the early spring of 1931; both tests were entirely negative at these times. In the summer of 1931, a low grade uveitis again developed in both eyes, and the patient reported with vision reduced to 20/100 in the right eye and 20/40 in the left eye. Examination showed faintly positive aqueous rays and fine deposits on the posterior surface of both corneas. The patient was again tested with lens protein and uveal pigment. The lens protein test was still entirely negative. The uveal pigment test, however, was strongly positive. Pigment therapy was recommenced in October, 1931, and has been continued steadily to date. Under pigment therapy all signs of uveal inflammation in both eyes have entirely disappeared, and vision has risen to 20/70 in the right eye and 20/20 in the left eye.

The cases of these two patients are apparently identical in that a hypersensitivity to uveal pigment developed following operation. One of the patients likewise showed hypersensitivity to lens protein, but on the last attack of uveitis the hypersensitivity to pigment alone remained. In both instances the uveitis cleared following pigment therapy. In the first case, in which the therapy was kept up continuously over two years, there were no recurrences. In the second case, in which the therapy was intermittent, there were definite recurrences, associated with the return of hypersensitivity. While no absolute conclusions can be drawn from such isolated cases, it would appear, in the absence of other causal factors and in view of the remarkable results following the therapeutic administration of pigment, that the uveal inflammation was definitely

associated with the hypersensitivity to pigment. It seems quite possible that in both instances we were dealing with an allergic endophthalmitis due to a hypersensitivity to the organ-specific pigment of the eye. There is no pathologic material available for study, such as we have in group VII. The clinical evidence in these cases would indicate that allergic endophthalmitis due to hypersensitivity to uveal pigment may be a definite clinical entity, and that these operative cases are similar in nature to the five traumatic cases reported in group VII, in which hypersensitivity to uveal pigment was also present, associated with chronic noninfectious uveitis.

GROUP IX.—*Sympathetic Ophthalmia.*—There were twenty cases of sympathetic ophthalmia in the entire series. Two of these cases were included in our report of 1925. The remaining eighteen cases have been seen since that date. However, since the two early cases have been followed over the last five years, they are included in this report.

Nature of Initial Injury: In seventeen of the twenty cases the sympathetic ophthalmia followed a penetrating wound involving the uveal tract in the exciting eye. In two patients the sympathetic ophthalmia followed intra-ocular operations done elsewhere, and in one patient sympathetic ophthalmia developed after the extraction of a cataract in the Wilmer Institute.

Interval Between Injury and Outbreak of Sympathetic Disturbance: In nine patients the sympathetic disturbance was first noted at a period between from three to four weeks after injury. In three patients the interval between the injury and the outbreak of the sympathetic disease was from five to six weeks. In four patients the interval was between three and four months. In two patients the interval was six months. In one patient the interval was one year, and in one patient it was two years. The last two cases are especially interesting in that the exciting eye was removed in one instance eleven months after injury, and the sympathetic disturbance occurred one month after the enucleation of the exciting eye. In the last patient the enucleation was done two years after the injury, and the sympathetic disturbance developed three days after enucleation of the exciting eye.

In six patients in this series the first signs of sympathetic disturbance in the second eye were noted after the exciting eye had been removed. In five of these patients the onset of the sympathetic ophthalmia was from two to nine days after enucleation of the exciting eye. The last patient, a child of 5 years, was seen eighteen days after enucleation of the exciting eye, at which time there was a fully developed sympathetic uveitis, which had apparently begun within a week after the enucleation of the exciting eye. These figures would indicate that sympathetic

ophthalmia is still to be feared at least two weeks from the date of enucleation of the exciting eye.

Age Incidence: Nine of the patients were below the age of 12 years, the youngest being 2½ years. Eight were between the ages of 18 and 30. One patient was 50 years of age; one, 51, and one, 72. This illustrates the well known tendency of the disease especially to affect the young.

Pigment Hypersensitivity Test: In fifteen patients the intracutaneous pigment test was definitely positive when the patient was first seen, and in three patients it was negative when the patient was first examined, and only later became definitely positive. In the first of these patients the pigment test was negative at the onset of the disease. In this patient the clinical picture of sympathetic ophthalmia was confirmed by pathologic examination of the exciting eye; the sympathetic disease developed after enucleation of the exciting eye. In the second patient the pigment test was negative when the child was first examined, nine days after the first suggestive symptoms of sympathetic ophthalmia had developed. Three months later, however, it was definitely positive. In the third patient the uveal pigment test was negative on admission, three weeks after the onset of the sympathetic disease. Four weeks later the uveal pigment test was strongly positive. This development of a positive test after a previous negative test is not due to hypersensitivity produced by the first test, for we have made pigment tests on a large number of normal persons at repeated intervals and have been unable to produce a sensitivity in human beings by previous intracutaneous test injections. There is, therefore, a definite group of patients with sympathetic ophthalmia in which the development of pigment hypersensitivity is delayed, for in three patients in the acute stages of the disease the test was negative, later becoming positive. This would apparently indicate that in certain acute stages of the disease there may be a definite negative phase, just as negative tuberculin reactions may be found in certain acute stages of tuberculosis.

In two other patients in this series the pigment test was negative. In one of these patients the test was made during a violent exacerbation of the disease and was completely negative. There was no opportunity to repeat this test later to determine whether it subsequently became positive. The second patient had an old case of sympathetic ophthalmia and was from the Blind School; the condition had been entirely quiescent for fifteen years. In this patient it is probable that the hypersensitivity, if before existent, had been completely exhausted.

Effect of Pigment Therapy: Three of the twenty patients with sympathetic ophthalmia were seen in the late stages of the disease, fifteen, ten and four years after the outbreak of the disease. In all of these three patients the eyes were hopelessly lost. Two patients were given

the advantages of optical iridectomies, without any improvement in the condition. The third patient, in whom the disease was four years old, showed a phthisical, inflamed eye hopelessly lost. Pigment therapy was outlined for this patient in the hope that it might control the pain and inflammation in the diseased eye. We have no further information as to the subsequent outcome.

The remaining seventeen cases were seen in the active stages of the disease. Five patients were treated with the usual therapy and received no treatment with pigment. Twelve patients were treated at one time or another during the course of the disease with uveal pigment as a therapeutic agent. The clinical course and results may therefore be summarized in the following two groups.

Group 1, Patients Not Receiving Pigment Therapy: In the first of these patients the sympathetic disturbance was not considered beyond the point of sympathetic irritation, which cleared immediately after the removal of the exciting eye and without further treatment. In the second patient there was evidence of sympathetic irritation in the left eye following a penetrating wound of the right eye four months previously. The uveal pigment test was strongly positive. The patient was advised of this condition. He refused enucleation of the exciting eye, left the hospital against advice and returned to his home in West Virginia. There is a note on this patient's history from a local physician, stating that sympathetic ophthalmia subsequently developed, but efforts to ascertain the final outcome have been unsuccessful. There remained, therefore, three patients with active sympathetic ophthalmia in the Wilmer Institute who did not receive pigment therapy. These patients were treated with the usual local treatment, massive doses of salicylates, arsphenamine and nonspecific protein therapy, including injections of milk and diphtheria antitoxin. One patient received autoserum therapy. In all three cases the course was steadily downhill. The patients were finally discharged; at the last examination the eyes were completely lost and the patients were blind.

Group 2, Patients Receiving Pigment Therapy: Of the twelve patients who received pigment therapy, five were first seen with the disease in an advanced stage, vision being reduced to little better than light perception, and the eyes already appeared hopelessly lost. In three of these patients the therapy had no beneficial results, and the disease ran its full fatal course. In the remaining two of these five patients the pigment therapy appeared to be attended with a rather rapid subsidence of the inflammation, but in both cases phthisis occurred and the eyes were lost. Three other patients treated with pigment did remarkably well, the disease clearing completely with the preservation of 20/70, 20/30 and 20/15 vision, respectively, in the sympathizing eyes. The

ninth patient was one of those with a delayed development of the hypersensitivity to uveal pigment. This patient was treated with the usual therapy for three months, during which time vision fell from 20/20 to 20/100 and the eye showed marked organic changes. After the pigment test became positive, pigment therapy was commenced. Thereafter there was steady improvement in the inflammatory picture, but no improvement in vision. One month later all evidence of active inflammation had subsided, and the patient was discharged with 4/100 vision. In the tenth patient (whose case was previously reported in 1925) the disease was completely controlled, and the eye remained quite free from inflammation, with 20/40 vision, until early in 1930, when it was the site of a second accident, the patient being struck in this eye by a steel spring. After this a traumatic cataract developed. An attempt to remove the cataract was unsuccessful, and phthisis finally occurred. The eleventh patient had a case of sympathetic ophthalmia of four months' duration, which had followed an intra-ocular operation on the fellow eye. The patient was given pigment therapy; the inflammation in the eye subsided and the cataract in the sympathizing eye was later extracted. A dense cyclitic membrane was encountered, however, which subsequently closed the pupillary opening. When last seen the patient had only light perception in this eye. The twelfth case was one of sympathetic ophthalmia following the extraction of a cataract. Pigment therapy was instituted two months after the onset of the disease, the eye having pursued a steady downhill course under the usual therapy. The inflammation in the sympathetic eye was apparently controlled. The eye was later operated on for extraction of the cataract that had formed, but again a cyclitic membrane was encountered, which closed the pupillary space, and efforts to open this have up to now been unsuccessful.

Summarizing the results of treatment with uveal pigment, there were five cases in which the eyes were hopelessly lost when first seen. In none of these cases were any beneficial results obtained, although in two cases the institution of pigment therapy seemed to be followed by a diminution in the inflammatory process. In three of the remaining seven cases, the patients did brilliantly, with the complete subsidence of the disease and preservation of useful vision. In another patient the disease was apparently controlled and useful vision was maintained for six years, but the eye was finally lost after a second accident. In one case the sympathizing eye was totally lost. In the remaining two cases the inflammatory stages of the disease were apparently well controlled, and the sympathizing eyes stood extraction of a cataract well. In both cases, however, cyclitic membranes were encountered, which subsequently closed the pupillary space.

Pathologic Picture in the Exciting Eyes: Of the twenty patients whose cases are reported in this series, there were three in whom the exciting eye was not removed. One of these was an old case of fifteen years' duration in a patient from the Blind School. When the other two patients were first seen in this clinic, the disease was so far advanced that the removal of the exciting eyes did not appear justifiable. In the remaining seventeen cases, thirteen of the exciting eyes had been removed in other clinics. All efforts to obtain sections and pathologic reports in these cases have been unsuccessful. There remain four patients from whom the exciting eyes were removed in this clinic, and the eyes were available for histologic examination. Three of the enucleated eyes showed the characteristic and well known picture of sympathetic ophthalmia: mononuclear and epithelioid cell infiltration and giant cells. The remaining case is most remarkable. The patient was a child, aged 7, who, after a penetrating wound through the cornea ran a violent course of definite infection in the eye, which was enucleated on this account. About eight days after the enucleation a typical and classic sympathetic ophthalmia developed, which ran a rapid downhill course, resulting in blindness. Examination of the enucleated eye showed a generalized, purulent endophthalmitis, with none of the characteristic findings associated with sympathetic ophthalmia. This case is in conflict with the generally accepted view that sympathetic ophthalmia does not follow purulent infections in the exciting eye. It appears probable that in this instance, as the sympathetic disease did not occur until eight days after enucleation of the exciting eye, the sympathetic process in the exciting eye may have been in an extremely early stage, and that the sympathetic picture, if then characteristic, may have been masked by the violent generalized infection. In any event, it is remarkable in being a clearcut case of sympathetic ophthalmia following a purulent infection of the exciting eye.

Nature of the Intracutaneous Pigment Reaction: Dr. Jonas Friedenwald made the interesting suggestion that study of skin into which pigment was injected might perhaps show a difference between the negative and the positive reactions, and, likewise, some difference might exist between the "true" positive and the "false" positive reaction. In the light of this suggestion, in collaboration with Dr. Friedenwald, an investigation of the histologic picture of the intracutaneous pigment reaction has been undertaken. This study has not yet progressed to the extent that any conclusive report can be made. However, the study thus far has shown an interesting finding which may ultimately throw some light on the question of the essential reaction to pigment in the allergic person.

We have removed skin into which pigment has been injected from a number of persons, at various times after the injection. This excision of the skin was all done under local injection of procaine hydrochloride. Unfortunately, the congestion and edema of the tissue that might result from a vascular reaction to pigment have necessarily been obscured as the result of the injection of procaine hydrochloride. However, in five normal persons and in one case of sympathetic ophthalmia with a clinically positive intracutaneous test to pigment the tissue was removed about twenty-four hours after the injection of pigment. There was no essential difference between the normal controls and the patient with sympathetic ophthalmia and the demonstrated allergy. The pigment was found infiltrated with monocytes and lymphocytes, and there was a varying degree of perivascular infiltration in the surrounding tissues. The actual extent of congestion and edema in the positive skin test, if present, was entirely obscured by the injection of procaine hydrochloride, as already mentioned. It will be necessary to repeat this study in persons in whom the tissue has been excised under general anesthesia in order to clear this point.

In two normal persons, skin into which injections were made was excised two weeks after the injection of pigment. These tissues showed a moderate infiltration with monocytes and lymphocytes around the injected pigment. The larger part of the pigment remained free in the tissues not ingested by phagocytic cells. There was moderate perivascular round cell infiltration in the tissues, but the reaction in the main consisted chiefly of lymphocytes with occasional monocytes and a very occasional epithelioid cell.

In two persons with positive intracutaneous tests to pigment the skin was removed two and four weeks after the injection of the pigment. One of these patients had a definite sympathetic ophthalmia, while the other was a small boy (described in case 3, group VI) in whom there was a definite "false" positive reaction to the intracutaneous injection of pigment. Both of the positive skin tests showed essentially the same pathologic picture, radically different from that shown by persons with a negative skin test. The pigment deposits were definitely infiltrated with great numbers of epithelioid cells and giant cells in which the granules were phagocytosed. No free extracellular pigment was found. The surrounding tissue showed intense perivascular round cell infiltration. The specimen of skin obtained from the patient with the false positive reaction showed an identical histologic picture with the exception of considerable amounts of newly formed fibrous tissue. In this patient, however, the skin was removed about four weeks after the date of injection, and the presence of this fibrous tissue may well be attributed to the longer duration following injection.

The difference in the cutaneous pathologic picture two weeks or more after the injection of pigment, in the patients allergic to pigment and those not allergic to pigment, was quite marked. In the two patients hypersensitive to pigment epithelioid cells and giant cells predominated, presenting a picture in the skin strikingly like the essential pathologic picture found in the eye in actual sympathetic ophthalmia. In the patients not hypersensitive to pigment the cutaneous reaction was essentially an infiltration with monocytes and lymphocytes, with only rare epithelioid cells and no giant cells. We realize, however, that we have only two late positive skin tests and two late controls, and that no possible conclusions can be drawn at the present time. However, while this subject requires further study before any final report can be made, the difference in the cutaneous histologic picture between those sensitive and those insensitive to pigment is most interesting.

COMMENT

When the group of one hundred and fifty-three patients is analyzed, the first noteworthy finding is that positive pigment tests were found only in patients in whom there had been a penetrating wound of the eye, either operative or traumatic. The second noteworthy finding is that the development of a positive pigment test usually indicates a gloomy prognosis. Of the thirty-two cases with positive pigment tests, eighteen occurred in sympathetic ophthalmia, five in low grade, delayed postoperative uveitis, in which three of the eyes were lost and two were apparently saved by pigment therapy, five in penetrating wounds of the eye in which the clinical course was steadily downward, so that enucleation was finally indicated from the clinical picture alone, and one in a penetrating wound of the eye in which the pathologic diagnosis was endophthalmitis phaco-anaphylactica, but in which the eye went steadily downhill until enucleation was indicated. Only in three instances was there normal recovery of the eye. In two of these instances the test was doubtfully positive. The third patient showed a strongly positive reaction, and this one case is the striking exception in the entire group.

The five patients in group VII, in whom positive intracutaneous pigment tests developed, and the five patients in group VIII, in whom a delayed, low grade, postoperative uveitis developed synchronous with the development of positive intracutaneous pigment tests, appear to belong to the same general group and to constitute in themselves a heretofore unrecognized clinical entity. These patients all have in common the development of a delayed, nonpurulent, chronic and recurrent uveitis, following either injury or operation on the affected eye, and, synchronous with the occurrence of this delayed uveitis, the development of a definite allergy to pigment. The eyes of four of the patients in group VII were available for pathologic examination, and three of these showed a picture

differing from that usually seen in nonspecific, noninfectious, chronic, traumatic uveitis. Two of the patients in group VIII were treated with pigment, and the eyes recovered. In the eight other patients, in spite of all usual local and general therapy, the eyes progressed either to enucleation or to blindness. It seems quite probable that these ten cases may represent an endophthalmitis dependent on the development of allergy to uveal pigment and a clinical entity somewhat similar to the endophthalmitis phaco-anaphylactica originally described by Verhoeff and Lemoine.[27] The possible assumptions are that the condition may be an inflammatory reaction due directly to pigment allergy, or that the development of the allergy to pigment may so impair the immune-biologic defense mechanism of the eye that normal healing becomes impossible.

Study of the group of patients with sympathetic ophthalmia, in the light of the group just mentioned, cannot but alter somewhat our conception of the allergic basis of sympathetic ophthalmia, as originally expressed by Elschnig, that in its essence it is an allergic reaction in the sympathizing eye due to the absorption of uveal pigment. Undoubtedly the development of pigment hypersensitivity in the course of the disease is usual, if not the rule, in sympathetic ophthalmia. Eighteen of our twenty patients showed such a pigment hypersensitivity, and it is quite probable that one of the other two cases was encountered in a negative phase, and, in view of our experience with other patients, might have been expected to have been positive at a subsequent examination, which was not possible. The twentieth case may be discarded for the reason that the sympathetic ophthalmia had been entirely quiescent for fifteen years, and it is highly probable that any sensitivity present would have subsided during that period. True hypersensitivity to uveal pigment results only after penetrating wounds of the eye involving the uveal tract. In our experience we have only one definite instance in which the development of such pigment hypersensitivity was followed by normal healing. In all other instances either a progressive low grade endophthalmitis or a frank sympathetic ophthalmia occurred. As we have eleven instances of the development of pigment hypersensitivity without sympathetic ophthalmia, it is quite probable that such a hypersensitivity to pigment is not the sole cause per se of sympathetic ophthalmia. This appears to indicate that some additional factor is involved in the development of a sympathetic disease. What the nature of this unknown additional factor may be can only be surmised: There may be differences in the degree of allergy; lysins acting on the chromatophores may be present, or an unknown infectious agent may enter into the picture. In the last instance, we might assume that

27. Verhoeff, F. H., and Lemoine, A. N.: Endophthalmitis Phaco-Anaphylactica, Internat. Cong. Ophth., 1922, p. 234.

alteration in the normal immune-biologic defense mechanism of the eyes follows the development of hypersensitivity to uveal pigment, and that this alteration in the defense mechanism makes it possible for the infectious agent thus to produce the characteristic disease.

This is in line with the idea advanced in 1925, that allergy to pigment might not be the only cause of the disease, and is not in conflict with the idea advanced later by Key, Marchesani, Riehm and others, that the development of elective sensitivity in the sympathizing eye is necessary to allow some specific infectious agent to produce sympathetic ophthalmia. Just what this other specific agent may be we do not know. There is some indication that it may belong to the general group of filtrable ultramicroscopic agents, but conclusive proof of this is lacking.

It appears that specific treatment with uveal pigment, when a definite hypersensitivity to pigment has been demonstrated, is of value. Certainly, in our experience the patients with sympathetic ophthalmia treated with uveal pigment have done vastly better than those not treated with pigment. Yet, it is equally true that treatment with uveal pigment is not a specific for the disease, for, as indicated in the body of this paper, there have been some cases in which treatment was apparently of no avail. In general, the beneficial effects that have followed pigment therapy are quite in accord with the idea expressed in the preceding paragraphs. Whatever may be our assumption of the real nature of the disease, pigment therapy is an attack on one phase of sympathetic ophthalmia. If sympathetic ophthalmia is due to an infectious agent that can operate only when the normal immune-biologic defense mechanism is impaired by the development of a hypersensitivity to pigment, the desensitization of the patient to pigment might well be expected to restore to normal such a defense mechanism. This is a plausible explanation for the clinical improvement observed after pigment therapy. It may likewise explain the beneficial effects observed in the two cases of low grade, noninfectious, postoperative cyclitis which were in group VIII, and which have already been reported.

SUMMARY AND CONCLUSIONS

One hundred and fifty-three patients with various ocular conditions have been tested with the intracutaneous pigment test. Thirty-two of the tests were positive and one hundred and twenty-one were negative. Hypersensitivity to uveal pigment was observed only after penetrating wounds of the eye. In general, the development of such hypersensitivity appeared to indicate a grave prognosis. Only one patient with a frank pigment hypersensitivity showed normal healing. One group of patients appears to present a new clinical entity: the development of a delayed noninfectious, recurrent and chronic, postoperative or traumatic uveitis, associated with the development of allergy to pigment. In sympathetic

ophthalmia hypersensitivity to pigment is a general rule, although patients with acute exacerbations of the disease may have a definite phase in which the intracutaneous test is negative. The development of pigment hypersensitivity does not appear to be the cause per se of sympathetic ophthalmia. This study indicates that some other factor enters into the disease. The nature of this additional factor is unknown. It may be that there are differences in the immune response of different persons, or allergy to pigment may alter the normal immune-biologic defense mechanism of the eye in such a manner as to allow some other specific agent to produce the characteristic picture of the disease. Therapy with uveal pigment, in patients who show positive intracutaneous tests, appears to be of real value. An explanation for such beneficial effects may be that desensitization with pigment allows the restoration of the normal immune-biologic defense mechanism.

ABSTRACT OF DISCUSSION

DR. PARKER HEATH, Detroit: Nine kinds of clinical groups are made in this study. Positive skin response to pigment tissue extract occurred only in those groups with penetrating wounds of the eye. These penetrating wounds were from accidental or surgical intervention. These extraordinarily interesting observations are emphasized in group VIII and partly in group VII, wherein positive skin reactions to pigment tissue extract occurred synchronously with inflammatory changes in the uvea. The mechanical injury obviously establishes a state of sensitization. The mechanism of what takes place from injury is not so obvious. It would seem either that material is carried in or that tissue and cellular relations are disturbed sufficiently and in a particular way to produce antigens. In other words, there is produced an overwhelming immune response, so that a defensive mechanism becomes pathologic and vicious. The nature of the allergic response, while increasingly important in current medical literature, is sufficiently unknown so that one may be justified in some speculation in this field. The authors have shown that sensitization to the uveal tissue pigment extract is the usual thing in sympathetic ophthalmia but that sensitization exists, not uncommonly, apart from this disease entity. The particular local feature in sympathetic disease is the cellular response in the uvea. Be the existing cause what it may—filtrable virus, protein degeneration product, metastatic material, or local tissue débris sensitizing electively—the reaction is an overwhelming cellular response. The initiating lesion may be small, but the immune response may completely overshadow it. Such a cellular response as is found in sympathetic disease is not unlike similar reactions in reticular tissue elsewhere in the body. The so-called reticular endothelial system, presumably with its important rôle in immune reactions and the production of antibodies, has been suggested in recent literature as the evil genius in many pathologic states, including sympathetic disease. The clinical fact that children are prone to sympathetic ophthalmia and to exaggerated effects from disease of reticular tissue may not be a coincidence. The differences in appearance of the sections taken from sensitized areas of skin may be explained by differences in age of the process. Such an explanation is satisfactory in the storage process of lipids by histiocytes. The pigment material of Drs. Woods and Little may not be free from other tissue substance. It is nearly impossible to free such minute and complicated structures from clinging foreign substances. Unfortunately, synthetic uveal pigment is not available.

The group showing late uveitis with sensitization to pigment tissue extract after operation or after trauma may be a clinical entity. A larger series with the same observations and without conflict in the matter of sensitization is necessary to establish it. The observations of the authors concerning the value of pigment tissue in prognostic tests is important. The use of the same material in treatment is hopeful.

DR. JONAS FRIEDENWALD, Baltimore: If this theory is correct, then one should be able to find granules of pigment in the centers of the inflammatory foci in the disease. Such a conclusion is analogous to Kock's postulate that the specific bacterial cause of a disease must be discoverable in the specific lesions of the disease. Recently I have investigated twenty cases of sympathetic ophthalmia histologically. In ten of these small, tubercle-like nests of epithelioid cells were found in the retina, and these epithelioid cell nests always contained melanin granules. This observation raised the question as to how far the characteristic inflammatory reaction of sympathetic ophthalmia might be considered as due solely to an allergic reaction to the pigment granule. The question can be answered by studying the histology of the reaction in the skin to a local injection of a suspension of uveal pigment. By studying the histology of the reaction in the skin to a local injection of a suspension of uveal pigment, it was found that the most characteristic differences in the histology of the skin test to uveal pigment appeared about two weeks after injection. Normal persons in general show only a moderate lymphocytic and monocytic infiltrate around the deposit of pigment, many granules of which remain unphagocytosed even after two weeks. In patients with cured sympathetic ophthalmia the intensity and character of the infiltrate were no greater than normal, but all the pigment was phagocytosed, indicating a higher opsonic index for pigment in cured sympathetic ophthalmia than in normal eyes. Whether this higher opsonic index is necessarily associated with the cure or is merely a result of the course of injections of uveal pigment which this patient received cannot as yet be determined. In contrast to the insignificant inflammatory reaction found in normal persons and in those with cured sympathetic ophthalmia, the one active case which we have so far studied showed a most intense inflammatory reaction with epithelioid cells and giant cells as well as lymphocytes. The histologic features of this reaction are indistinguishable from the characteristic lesions of sympathetic ophthalmia. While not enough cases have as yet been studied to enable final conclusions, this observation seems to me to afford strong support to the Elschnig-Woods theory that allergy to uveal pigment is an integral part of the etiology of sympathetic ophthalmia. I think that the further conclusion can be drawn that allergy to uveal pigment suffices to explain the characteristic histologic features of the disease.

EFFECT OF REACTION ON OPHTHALMIC SOLUTIONS

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The effect of drugs introduced into the conjunctival sac in the form of solutions is modified by a number of factors. One of the most important of these is their immediate dilution by tears always present in the sac and by those which rapidly reach it in response to the stimulation afforded by any chemical irritant. A second factor is precipitation of the drug substances present in the tears or conjunctival secretion or its chemical union with such substances. This is especially important when large amounts of highly albuminous secretion are present, as may easily be seen by the white precipitate of silver albuminate which forms when silver nitrate is applied to lids covered with purulent secretion. Such combination, of course, renders most of the drug inactive.

A third factor is that of the reaction of tissues and tears and of the solutions employed. Lipschütz [1] showed that the zinc salts are precipitated in alkaline solutions, and that when a neutral solution of these salts comes in contact with the tears, the reaction of which is about p_H 8, immediate precipitation occurs, rendering the drug inactive. This he was able to prevent by using zinc salts in a medium of p_H 5.5, which is acid enough to neutralize the slightly alkaline lacrimal fluid. He also found that the reaction of the commonly used collyria is the chief factor in the irritation felt when they are introduced into the sac. Physiologic solutions of sodium chloride with a p_H from 8 to 7 produced no sensation. Solutions slightly acid (with p_H of from 6.6 to 6.3) or slightly alkaline (p_H 9) produced a slight feeling of irritation, and some congestion. More acid solutions (with a p_H of from 6 to 4.5) produced severe burning and congestion. He found that reaction played a far greater rôle than the osmotic pressure of the solution, which has generally been considered more important. If the reaction was kept at p_H 7.6, solutions of sodium chloride from 0.3 to 1.5 per cent produced no irritation. The tears themselves are slightly hyper-

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1. Lipschütz, H.: Klin. Monatsbl. f. Augenh. **82**:763, 1929.

tonic, containing 1 per cent of sodium chloride. In solutions the reaction of which is adjusted by simple acids or alkalis, this reaction is modified rapidly on contact with air or tissue fluids. Hence, Lipschütz proposed the use of buffer solutions containing a combination of salts which dissociate in such a way as to give any desired reaction and which protect the solution against slight changes of reaction.

Von Pelláthy and Schneider [2] estimated the reaction of the conjunctiva itself in the normal state and in various pathologic conditions. They found the normal conjunctival secretion to have a reaction of from p_H 7.2 to p_H 7.4, while in trachoma and certain forms of chronic conjunctivitis the reaction became more acid, from p_H 6.8 to p_H 6.9. They tried the effect of modifying this reaction by the use of alkaline collyria, using 5 per cent sodium carbonate by frequent instillation and 8 per cent ointment. They reported marked relief of symptoms in many cases after such treatment. Lusza,[3] however, tried the same method of treatment in such cases without effect.

According to recent work by Fischer,[4] the reaction of solutions is an important factor in the absorption of drugs by the cornea, through which nine tenths of the substances reaching the interior of the eye after instillation must pass. By rather complicated micromethods of analysis, he estimated the amounts of certain alkaloids recoverable from the aqueous after bathing the eye in solutions of these drugs of varying reactions. He found that pilocarpine was absorbed best at a p_H of from 4 to 5, while atropine, physostigmine (eserine) and scopolamine were absorbed poorly in acid solutions and best at p_H 7.5.

In an attempt to estimate the importance of this factor of reaction, we tested the reaction of various solutions commonly employed and the behavior of the drugs in solutions of varying reaction, and observed the clinical effects of such solutions. As a medium for preserving the desired reactions, the buffer solution described by Fischer, containing sodium bicarbonate and potassium chlorate, was first used. This was found to become rapidly acid on exposure to air, owing to the absorption of carbon dioxide. It was desirable that the ideal buffer solution should inhibit the growth of bacteria and fungi, so boric acid was chosen as one constituent. Since Antonibon [5] had claimed that potassium chloride showed a synergistic action when added to solutions of the alkaloids, and since the salt is an effective neutral buffer, it was also employed. The buffer solution was made with the advice of Dr. Henry I. Stubblefield of the Department of Bacteriology.

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2. von Pelláthy, B., and Schneider, K.: Klin. Monatsbl. f. Augenh. **85**:774, 1920; **86**:113, 1931.

3. Lusza: Klin. Monatsbl. f. Augenh. **87**:769, 1931.

4. Fischer: Klin. Monatsbl. f. Augenh. **86**:298, 1931.

5. Antonibon, A.: Ann. di ottal. e clin. ocul. **57**:134, 1929.

Solution 1, the acid buffer solution, was made as follows:

Boric acid	6.2 Gm.
Potassium chloride	7.4 Gm.
Distilled water	1,000 Cc.

The reaction of this solution is p_H 5.5.

Solution 2 is a fifth-molar solution of sodium carbonate, containing 21.2 Gm. of sodium carbonate (Na_2CO_3) to the liter of distilled water. This solution is used only in making solution 3, the alkaline buffer solution. One cubic centimeter of solution 2 is added to 50 cc. of solution 1 for this solution, which then has a reaction of p_H 7.6. Although it will be referred to as an alkaline buffer solution, it is, of course, almost neutral, being less alkaline than the tears.

The reaction of some drugs commonly employed, prepared in distilled water, estimated by the Clarke and Lubs method, was as follows:

	p_H
1 per cent atropine sulphate	5.8
2 per cent homatropine hydrobromide	5.5
2 per cent cocaine hydrochloride	4.6
1 per cent pilocarpine nitrate	4.8
0.2 per cent physostigmine sulphate	6.6
1:1,000 nupercaine	4.4
4 per cent procaine hydrochloride	4.6
1:1,000 epinephrine	4.6
2 per cent butyn sulphate	5.4
0.9 per cent sodium chloride	7.0
0.2 per cent zinc chloride	5.0
Boric acid, saturated solution	4.2

When the foregoing drugs were made up in a saturated solution of boric acid, their reactions varied from p_H 4.2 to p_H 5. Boric acid in saturated solution (p_H 4.2) is not so irritating as would be expected from Lipschütz's article, the slight burning sensation produced being about the same as that caused by the acid buffer solution described. Solutions of most alkaloids in this medium produce about the same sensation as that caused by the medium itself. The exceptions are the later cramping sensation from miotics, the more intense burning from the first drop of butyn or phenacaine and a peculiar immediate cramp-like sensation caused by 1:1,000 epinephrine.

While the irritation caused by the boric acid solution and by the alkaloids in distilled water, which have an acid reaction, is slight, it is complained of by some persons. This feeling of irritation is entirely absent after the instillation of the alkaline buffer solution described. The only sensation after such an instillation is of the slight impact of the drop followed by that of an excess of fluid in the conjunctival sac. With most of the alkaloids in this solution, the sensation is the same,

except with the drugs mentioned, which are themselves irritating. The addition of these drugs in the strengths commonly employed to the buffer solutions does not modify their reaction more than p_H 0.2.

An advantage of the buffer solutions over physiologic solution of sodium chloride as a medium is that fungi and bacteria do not grow in them or do so only exceptionally. Solutions used with the ordinary dropper tops, which are exposed to air when used, remain clear for several months. Solutions of physostigmine in alkaline buffer solution turn red more rapidly than in saturated solution of boric acid, but this does not seem to affect their efficacy. The importance of protecting patients against needless contamination of their collyria by this or some other method hardly requires emphasis.

The solubility of the various drugs in solutions of varying reaction was studied, and this established certain practical rules, some of which are already well known, for making up solutions. Cocaine, zinc salts and epinephrine are insoluble in the alkaline solution, but are soluble in the acid buffer solution. Phenacaine is insoluble in the alkaline solution and in distilled water, but soluble in the acid buffer solution if it is made slightly more acid (p_H 4.8) by the addition of a few drops of dilute acetic acid to the ounce. These drugs, then, with the modification noted for phenacaine, may be used in the acid buffer solution if desired.

Atropine, homatropine, physostigmine and pilocarpine are soluble in both solutions, but, for reasons to be explained, have been employed in the alkaline solution.

Sodium fluorescein is insoluble in either solution, and dissolves only at p_H 9, which is approximated by a 2.5 per cent solution of sodium carbonate. Another derivative of fluorescein, which was first called to our attention by Dr. Harry Gradle, is soluble in distilled water, and a 1 per cent solution has the same staining properties as sodium fluorescein. Such a solution is practically nonirritating, while the alkaline solution of sodium fluorescein is distinctly irritating, and this difference would seem to be due principally to the difference in reaction. Both solutions remain free from gross bacterial and fungus growth without the addition of preservatives.

Metaphen, an organic mercury derivative used as an antiseptic, is insoluble either in buffer solution or in distilled water, but is soluble in a solution of p_H 8. This is the reaction of the 1 : 500 solution as it comes from the manufacturers, and dilutions suitable for instillation (1 : 2,500) are conveniently made by adding distilled water to the stock solution, the reaction remaining the same.

Butyn is insoluble in either buffer solution, but is soluble in distilled water. A 2 per cent solution of butyn in distilled water remains clear without the addition of any preservative, the drug itself having a defi-

nite bacteriostatic effect. (Fungi may grow in this solution if frequently exposed to air and 0.5 per cent chlorbutanol may be required to prevent this.)

The buffer solutions described, chiefly the alkaline solution, have been used in the clinic and in practice as a medium for drugs for about a year, and some observations on their use may be mentioned. Patients who complained of irritation from collyria in the saturated solution of boric acid which was formerly employed have noted distinctly less irritation when they are used in the alkaline buffer solution. This is especially true of patients using physostigmine, in spite of the unavoidable late cramping sensation produced by the alkaloid itself.

Some interesting observations on patients with idiosyncrasies were made. On using 1 per cent pilocarpine nitrate in acid buffer solution, a severe follicular conjunctivitis developed in one patient within a week, which subsided when the drug was changed to physostigmine. A patient in whom conjunctivitis developed when 0.2 per cent physostigmine in boric acid solution was used was given the drug in alkaline buffer solution, but a similar conjunctivitis developed. Another patient, however, who had been unable to use physostigmine because of conjunctival irritation is using it in alkaline buffer solution without any such symptoms. In a case of idiosyncrasy to atropine the drug used was tried in alkaline buffer solution, but its effect was the same. No cases of conjunctival irritation from pilocarpine in alkaline buffer solution have been seen. It may be concluded from these few cases that, while patients with a true idiosyncrasy are probably not affected by the reaction, the irritation caused by physostigmine is in some patients much diminished or entirely obviated when it is used in the alkaline buffer solution. It seems possible that reactions to pilocarpine are more apt to result from acid solutions. The irritating effects of old or contaminated pilocarpine solutions may be due in part to the formation of acid by bacteria and molds.

In the work by Fischer previously referred to, no observations were reported on the clinical effects of such differences in absorption as he observed. We tested the alkaloids homatropine, physostigmine and pilocarpine in acid and alkaline solutions, attempting to determine whether the speed and duration of the pupillary response were influenced by the reaction of the medium. Ten normal patients were employed with each drug, the time required for the first measurable pupillary response, that for maximal pupillary response and that for a return to normal being recorded. With 1 drop of 1 per cent pilocarpine nitrate in alkaline buffer solution, the average time before the first response was ten minutes, while with the acid buffer solution it was twelve minutes. The time before maximal miosis was twenty minutes with the alkaline and twenty-five minutes with the acid solu-

tion. The duration of miosis was about the same after both solutions, but was slightly longer in some cases with the alkaline solution.

Similar observations were made with 0.2 per cent physostigmine sulphate, the first reaction being seen in twelve minutes with the alkaline solution; maximal miosis appeared in twenty-three minutes and persisted for two hours. With the acid solution the first reaction was seen in fourteen minutes; maximal miosis appeared in twenty-eight minutes, and the miosis persisted for only one and one-half hours. With homatropine, mydriasis occurred so rapidly that no distinct differences could be recorded.

It will be seen that for physostigmine our observations would agree with those of Fischer, who reported increased absorption in alkaline solution. In the case of pilocarpine, however, the greater efficiency in alkaline solution could not be expected if Fischer's calculations of an increased absorption in acid solution are correct, unless some other factor than speed of absorption is used to explain our findings.

Comparisons were made between an alkaline buffer solution containing potassium chloride and one from which it was omitted, in order to test the synergistic action of potassium chloride which Antonibon described. No differences in the effects of the two solutions could be observed with any of the three alkaloids tested.

Acid solutions a month old were much less effective than fresh acid solutions. With the alkaline solutions there was some loss of efficiency after a month, but an old alkaline solution of physostigmine was still more effective than an acid solution freshly made up.

Following the report of von Pelláthy and Schneider, we used the alkaline buffer solution in a number of cases of chronic catarrhal conjunctivitis as a collyrium for instillation three or four times a day, without any attempt, however, to estimate the reaction of the secretion in such cases. In a number of cases the condition cleared up rather rapidly on such treatment, as rapidly or more so than in cases in which the patients were given the usual 0.2 per cent solution of zinc chloride. In two cases of the mild form of epithelial dystrophy with a definite deficiency in tears, frequent instillations of the alkaline buffer solution as a substitute for tears had a definitely favorable effect on the symptom of dryness, which might have been obtained equally well by physiologic solution of sodium chloride.

CONCLUSIONS

1. A simple form of buffer solution is suggested as a medium for eye-drops.

2. The acid solution is suitable for drugs soluble only in acid mediums, such as zinc, phenacaine, cocaine and epinephrine.

3. The alkaline solution is less irritating and is a suitable medium for atropine, homatropine, physostigmine and pilocarpine.

4. Certain alkaloids, such as physostigmine and pilocarpine, seem to be more effective in alkaline than in acid solution, while with others, such as zinc, the reverse is the case.

5. Conjunctivitis from physostigmine and pilocarpine probably occurs less often when they are used in alkaline solution.

6. Solutions of drugs in the buffer solution require no additional preservative.

7. The alkaline buffer solution alone is a nonirritating collyrium, suitable for cleansing the conjunctival sac and for replacing deficient tears.

OCULAR SYPHILIS

III. REVIEW OF THE LITERATURE AND REPORT OF A CASE OF ACUTE SYPHILITIC MENINGITIS AND MENINGO-ENCEPHALITIS WITH SPECIAL REFERENCE TO PAPILLEDEMA

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It is now known that the central nervous system is involved in a large percentage of patients in the early stage of syphilis. Such involvement may be expressed clinically as symptoms of acute meningitis and meningo-encephalitis in which papilledema may be a conspicuous symptom. Early neurosyphilis is therefore of interest to the ophthalmologist.

The purpose of this paper is a discussion of papilledema as an expression of acute syphilitic meningitis, an analysis of fifty reported cases and the report of a typical case.

Papilledema of syphilitic origin is almost invariably a symptom of acute syphilitic meningitis or meningo-encephalitis. The latter process may occur in the three following stages of syphilitic infection; more commonly during the secondary stage, either before, during or soon after the secondary exanthem, much less commonly as an acute exacerbation in congenital syphilis and in latent periods during the tertiary stage of acquired syphilis.

Acute syphilitic meningitis and meningo-encephalitis are relatively rare. Carr [1] found them twelve times in five hundred and thirty syphilitic patients. He stated that papilledema was the most common objective symptom in the twelve cases. Nonne [2] encountered five cases. The majority have been reported by the French.

There is a much greater frequency in males than in females, the disease occurring in the ratio of 4 to 1. The process develops more commonly in young adults, but may occur in infancy or late years.

From the Clinic for the Treatment of Ocular Syphilis, Wills Hospital; J. V. Klauder, M.D., Director.

1. Carr, A. D.: Acute Syphilitic Meningitis, Am. J. Syph. **13**:360 (July) 1929.

2. Nonne: Acute Meningitis in Early Syphilis, Med. Klin. **17**:1501, 1921; abstr., J. A. M. A. **78**:768 (March 11) 1922; Early Acute Forms of Neurosyphilis, Rev. méd. d. Uruguay **26**:350, 1923; abstr., J. A. M. A. **81**:1826 (Nov. 24) 1923.

In 1913, Hutinel [3] stated that syphilitic meningitis occurs in infants associated with such specific lesions as roseola, a hard liver and spleen and changes in the bones. He quoted another example of this condition observed by Ravaut in an infant 3 weeks of age who presented scattered syphilids over the trunk and face, and had a hard liver and spleen. The diagnosis was confirmed at necropsy.

Mazzeo [4] reported four cases in children between 5 and 24 months of age. Lavergne [5] cited two cases in children of 3½ and 9 years of age, respectively, with positive serologic pictures. Ström-Olsen [6] described a case occurring in juvenile dementia paralytica. Vasiliu [7] cited three cases in children whose conditions had previously been diagnosed as tuberculous meningitis. These patients presented stigmas of congenital syphilis and, in addition, positive Wassermann reactions.

The period elapsing between the appearance of the primary lesion and the onset of the disease varies. In the case reported by Neumann [8] it was two and one-half months; in those reported by Pette, three and nine months; in that reported by Wilson and Gray,[9] three months; in those reported by Krause (quoted), three and seven months, and in the case reported by Fahr, nine weeks.

Trauma plays no definite rôle in this condition, although there have been cases reported following injury. Smith [10] reported four cases occurring in the latent stage following trauma.

PATHOLOGY

According to Jakob,[11] this form of meningitis presents its most characteristic form in the early secondary stage. It is characterized by a diffuse, small cell infiltration of the pia-arachnoid in which lymphocytes predominate. Plasma cells are few in number or are missing

3. Hutinel: Les méningites syphilitiques, Rev. gén. de clin. et de thérap. **27**:437, 1913.

4. Mazzeo, A.: Acute Syphilitic Meningitis, Pediatria **34**:299, 1926; abstr., J. A. M. A. **86**:1666 (May 22) 1926.

5. Lavergne, M.: Méningitis syphilitiques et réactions méningées chez des syphilitiques, Arch. de méd. d. enf. **19**:579, 1916.

6. Ström-Olsen, R.: A Case of Congenital Syphilis with Syphilitic Meningitis, Lancet **2**:78 (July 12) 1930.

7. Vasiliu: Indépend. méd. et méd. orient. **16**:579, 1912.

8. Neumann, J.: Zur Meningitis acuta syphilitica, Zentralbl. f. inn. Med. **39**: 609, 1918.

9. Wilson, S. A. K., and Gray, C. E.: Acute Syphilitic Meningitis, Brit. M. J. **2**:419 (Sept. 29) 1917.

10. Smith, E. R.: Tryparsamide in Acute Luetic Meningitis, Am. J. Syph. **11**:432 (July) 1927.

11. Jakob, A.: Normale und pathologische Anatomie und Histologie des Grosshirns, Leipzig, Franz Deuticke, 1927, vol. 1.

entirely. In severe cases polymorphonuclear cells are present, but are soon replaced by lymphocytes. The intensity of the infiltrative process varies greatly. For the most part it occurs around the blood vessels, producing infiltration, intimal proliferation and inflammatory changes, but without degeneration. After a certain period hyperplastic connective tissue invades the meninges. The meningeal involvement is commonly present over the cerebrum, especially in the region of the chiasm and the sylvian fissures. It also involves the brain stem and circumference of the spinal cord. Not uncommonly the cerebral and cerebellar convexities, as well as the ventricles, are involved. The infiltration follows along the path of the larger vessels into the brain tissue. There is frequently a penetration of the exudative process into the marginal zones of nerve tissue with the formation of encephalitic areas. The cranial nerves, especially the optic and auditory, are often markedly infiltrated with lymphocytes and plasma cells. This infiltration accumulates not only in the sheaths but also in the nerve tissue itself. The spirochetes are not always found. They may be seen in the meninges, the lumens of the blood vessels and the marginal zones.

The vessel walls, aside from adventitial infiltration, may be quite normal, but usually show severe changes, especially in long-standing cases. The adventitia and media are involved, the elastic lamina splits, and the intima proliferates. In those cases in which the process develops in latent forms there are, of course, chronic changes in the vessels.

The end-results of this process may be the regression and disappearance of the inflammatory elements corresponding to a clinical cure, or chronic changes may result if death does not occur.

SYMPTOMATOLOGY

Acute syphilitic meningitis may begin abruptly or gradually. It is almost always ushered in by headache, which is constant and severe and tends to show acute exacerbations. It is not always worse at night. There are usually nausea and vomiting. Fever is present in less than one half of the cases. When present, it varies from 99 to 103 F. Cervical rigidity is almost always present and varies in degree of severity. Diplopia is often present. The pathologic reflexes and Kernig's sign are commonly present. Aphasia, when it occurs, is usually transient. Generalized convulsions are not common and occur for the most part in children.

In most cases the pupils show some abnormality. They are often irregular and unequal. The Argyll Robertson pupil is found in approximately one fourth of the cases, but the majority show a sluggish reaction to light. The optic nerve is commonly affected. There may be a papillitis or a papilledema. When the latter is present, it is usually

bilateral and varies in degree from 2 to 5 diopters. The visual fields usually show a general concentric contraction for form and color. Choroiditis and retinitis occur. The oculomotor, abducens, facial and auditory nerves are more commonly involved than the others. This involvement is more often unilateral. There is a more pronounced involvement of the cranial nerves in the cases with concomitant meningo-encephalitis.

Delirium or coma may be the first sign of this disease. Some mental disturbance is almost always present at some time during the course. It may vary from a mild depression to an acute mania. Mental irritability and confusional states are common. Loss of memory is a prominent symptom.

The serologic findings in syphilitic meningitis are of the utmost importance. The Wassermann reaction of the blood is positive in about 85 or 90 per cent of cases. The Wassermann reaction of the cerebrospinal fluid is positive in 100 per cent of cases. If the Wassermann reaction of the cerebrospinal fluid is negative on several successive examinations, the diagnosis of acute syphilitic meningitis is probably incorrect. Polleri [12] has reported a case, however, in which both the blood and the cerebrospinal fluid were negative, and the patient recovered following antisyphilitic therapy. The manometric pressure of the cerebrospinal fluid is slightly increased in the majority of cases. The fluid is from clear to turbid and faintly yellow, and it usually contains a fibrin clot. The number of cells in the cerebrospinal fluid is of diagnostic import. It is always increased over the normal in this condition. The cells are largely or entirely lymphocytic in type. Polymorphonuclear cells, however, may be present in the more severe cases early in the disease. The total cell count varies from 10 to 1,500 cells per cubic millimeter. The protein is always increased in amount. The chlorides and sugar content may be normal or slightly decreased.

The colloidal gold curve, which is not constant, may be of the syphilitic or paretic type. Spirochaeta pallida have been found in the cerebrospinal fluid in this disease.

The diagnosis of acute syphilitic meningitis is based first on a history of syphilis in the patient or the parents. Signs of acquired or congenital syphilis may aid. This condition cannot be accurately diagnosed without the serologic findings. When these are indicative of syphilis, together with a history and symptoms of syphilis and meningitis, the diagnosis of syphilitic meningitis can be made with certainty. The presence of Spirochaeta pallida in the cerebrospinal fluid is pathognomonic. Tuberculous meningitis is most often confused with syphilitic

12. Polleri, P. M.: Acute Gumatous Meningitis, Policlinico **30**:1313 (Oct. 8) 1923; abstr., J. A. M. A. **82**:165 (Jan. 12) 1924.

meningitis. In the differential diagnosis, acute encephalitis, purulent meningitis and the many toxic states producing meningeal irritation should be considered. When papilledema is present, tumor of the brain, cerebral abscess, cerebral hemorrhage, sinus thrombosis and lead encephalopathy should also be considered.

The prognosis is good if a diagnosis is made early and antisyphilitic therapy is instituted at once. However, Nonne [2] cited one case of his own and one reported by Fahr in which the symptoms were mild and yet both patients died after antisyphilitic therapy.

ANALYSIS OF FIFTY CASES

Of the fifty cases reviewed from the literature, forty occurred in male patients. The average age was 27.2 years; the youngest patient was 1 year and the eldest 49 years of age. The mortality was 22.2 per cent. (With modern intensive antisyphilitic therapy this mortality can be greatly reduced.) Autopsy was performed in five of the eleven cases in which death occurred, and in each substantiated the clinical diagnosis.

In nineteen cases there was no history of a syphilitic infection. In the remaining thirty-one cases, there was a history of a primary lesion in twenty-seven and signs of congenital syphilis in four. The average interval existing between the primary lesion and the onset of the disease was one and eighty-eight hundredths years. The shortest duration was two weeks, and the longest, twenty years. Eleven of the patients had had previous antisyphilitic treatment (arsphenamine, mercury or bismuth).

The Wassermann reaction of the blood was strongly positive in forty-five of the forty-eight cases in which the test was made. The Wassermann reaction of the cerebrospinal fluid was strongly positive in forty-nine of the fifty cases.

The average cellular content of the cerebrospinal fluid was 414 cells per cubic millimeter. The largest number found was 1,780, and the smallest was 16. The majority of the cells were lymphocytes. The globulin content was increased moderately in all cases. Spirochetes were found in the cerebrospinal fluid in two cases. The colloidal gold curve showed either a syphilitic or a dementia paralytic curve.

Papillitis was reported in eight of the fifty cases. Papilledema was present in sixteen cases. It was bilateral in fourteen and unilateral in two cases. It is probable that there would have been a higher incidence of papilledema had a fundus examination been made on all of the patients. In twenty cases no mention was made of involvement of the optic nerve. The degree of papilledema present in the sixteen patients ranged from 2 to 5 diopters.

Headache was the initial symptom in forty-six of the fifty patients. Of the other four, loss of consciousness was the initial symptom in one, mental irritability in a second, vomiting in a third and vertigo in the fourth.

Pupillary abnormalities were present in thirty-two cases. These abnormalities consisted of irregularity, inequality, disturbance of light reflex and the accommodation-convergence reaction. There were irregularity of one or both pupils in twelve patients, inequality in eleven, and Argyll Robertson pupils in seven.

It is both interesting and important to note that some observers believe that there has been an increase in the incidence of syphilitic meningitis since the advent of arsphenamine therapy. It is believed that the so-called neurorecidive is responsible for the acute syphilitic meningitis. Pfister [13] reported six cases following insufficient arsphenamine therapy.

The Symptoms and Their Incidence in the Fifty Cases

Headache	46
Nausea and vomiting	19
Mental disturbances	5
Disturbances of consciousness	13
Fever	18
Cranial nerve paralyses	24
Convulsions	4
Visual disturbances	8
Cervical rigidity	35
Kernig's sign	10
Babinski sign	6
Aphasia	3
Hemiparesis	2

The neurorecidive is the occurrence of symptoms of neurosyphilis, usually meningeal in character, appearing as a relapsing manifestation following insufficient treatment of early syphilis, more particularly with the arsenicals. The most frequent concomitant ocular lesions are optic neuritis, papillitis and involvement of the oculomotor, abducens or trochlear nerves.

Artz and Kerl [14] concluded that the neurorecidive is due to activating latent groups of spirochetes, since the organisms are found in the spinal fluid in patients with early syphilis. In 1911, Finger [15] reported 9 per cent neurorecidive appearing in the course of the treatment of five hundred syphilitic patients (mostly secondary cases) with arsphenamine. He stated that during the same period he encountered only five cases of neurorecidive among two thousand patients treated with mercury; that

13. Pfister, M.: Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:455, 1926.
14. Artz and Kerl: Wien. klin. Wchnschr. **27**:787, 1914.
15. Finger, E.: Med. Klin. **7**:1750, 1911.

its occurrence to the extent of 94 per cent was in the early period of syphilis, and that it did not occur in the presence of preexisting syphilitic disease of the central nervous system.

From the analysis of cases cited in this paper, one is impressed by the fact that only eleven of the fifty patients (22 per cent) had had previous antisyphilitic therapy. This fact is in direct opposition to the belief that acute syphilitic meningitis is an expression of a neurorecidive, especially of the arsenicals.

REPORT OF A CASE

History.—A white woman, aged 23, married, was admitted to the Clinic for the Treatment of Ocular Syphilis, Wills Hospital (in Dr. Griscom's service), on March 2, 1931, complaining of severe headache, dimness of vision, left facial weakness and general fatigue.

She had had no abortions or miscarriages, and there was no history of a primary lesion or a secondary eruption.

Three and one-half months before admission severe throbbing pain had developed over the occipital region, the posterior aspect of the neck and the frontal area. This was accompanied by fever, slight nuchal rigidity, nausea and vomiting. She was confined to bed off and on for seven weeks. At the end of this time she complained of failing vision in both eyes, weakness of the left side of the face, tinnitus and impairment of hearing in the left ear and inability to turn the left eye outward, with consequent diplopia. At about the same time she noticed numbness and tingling of the fingers of the right hand, which sensation passed upward to the right axilla and from the left foot to the left knee. She was then admitted to a hospital in an adjoining state for a period of eight weeks, where she received approximately thirty inunctions of mercury and potassium iodide by mouth. No intravenous or intraspinal injections were given. During this time the left facial paralysis improved, but the impairment in hearing persisted.

Neurologic Status.—There was a slight Romberg sign. The gait was somewhat uncertain owing to the vertigo resulting from the diplopia.

The optic nerves showed marked involvement. Vision on admission was 6/9 in the right eye and 6/20 in the left eye. There was a swelling of the nerve head of 2 diopters on the right, more marked in the lower quadrant. The retinal veins were distended. The margins of the disks were veiled and hazy. No hemorrhages or exudates were seen. On fundus examination the left eye showed a swelling of the nerve head of 4 diopters; there were no hemorrhages or exudates. The visual fields showed concentric contraction for form and color.

The pupils were regular but unequal. The left was larger than the right. Both reacted sluggishly to direct and consensual light stimulation. There was poor reaction to accommodation-convergence. The left eye showed weakness of external rotation and downward movement. The diplopia increased in the vertical meridian down and inward. There was a slight facial weakness on the left. The hearing was impaired on the left. There were no sensory disturbances. Both patellar reflexes were slightly exaggerated. There was a fine tremor of both hands on extension. No disturbance of cerebellar function could be elicited.

The serologic findings were as follows: On admission the Meinicke and Wassermann reactions of the blood were strongly positive. The cerebrospinal fluid showed 277 lymphocytes and a marked increase in globulin. The Wassermann and

Meinicke reactions of the cerebrospinal fluid were strongly positive. The colloidal gold test showed a syphilitic curve.

The clinical diagnosis was acute syphilitic meningitis and meningo-encephalitis.

Treatment and Course.—Potassium iodide in 15 grain (0.97 Gm.) doses was given by mouth three times daily. A course of twelve consecutive doses of 0.2 Gm. of soluble bismuth suspended in oil was given intramuscularly. Neoasphenamine was given in increasing dosage from 0.3 to 0.6 Gm. once each week. Intravenous injections of sodium iodide in 25 grain (1.62 Gm.) doses were given weekly. Spinal drainage was instituted for the relief of increased intracranial pressure. This treatment was continued for a period of three months, when the intravenous iodides were discontinued. The patient then had a course of twelve injections of neoarsphenamine alternating with another course of twelve intramuscular injections of bismuth for a period of five months.

One month after admission vision in the right eye was 6/8; that in the left eye was 6/12. The papilledema was reduced to a swelling of only 1 diopter in each eye. The patient still complained of severe headaches. Six weeks later, the diplopia was much lessened and the headaches were entirely absent. Two months afterward, there was only a slight haziness of the margins of the disks, and the hearing in the left ear was slightly improved. Two months later, there was no swelling of either disk. Vision in the right eye was 6/8; that in the left eye was 6/10. The diplopia was absent.

SUMMARY

1. Acute syphilitic meningitis and meningo-encephalitis are relatively rare, but their presence should be considered in any patient presenting signs of meningeal involvement.

2. Papilledema is an interesting and important clinical sign in this disease and should be searched for in all cases. It was present in sixteen of the cases reported. The degree of papilledema in these sixteen patients ranged from 2 to 5 diopters, and the swelling involved both optic nerves in fourteen cases.

Papilledema in this disease responds very well to antisyphilitic treatment; in some cases, however, a postneuritic atrophy remains.

3. Contrary to the opinion of many observers, this disease process develops often in those cases in which there has been no previous antisyphilitic therapy. Previous insufficient antisyphilitic therapy, especially arsphenamine, therefore, is not necessary for the development of acute syphilitic meningitis.

4. Headache, cervical rigidity and paralyses of the cranial nerves were the most prominent symptoms.

5. Acute syphilitic meningitis and meningo-encephalitis respond well to early and intense antisyphilitic therapy.

6. Fifty cases of acute syphilitic meningitis and meningo-encephalitis from the literature have been analyzed and one case reported with special reference to the presence of papilledema.

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NEW CONCEPTION OF DIOPTRIC POWER

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Students of physiologic optics, and this includes more or less every ophthalmologist, must have noted certain apparent discrepancies in the calculation of dioptric power as given in different works on the subject. For instance, in the classic work of Tscherning, the powers of the four refractive surfaces of the eye are given as follows:

Anterior surface of cornea, plus 47.24 diopters
Posterior surface of cornea, minus 4.73 diopters
Anterior surface of crystalline lens, plus 6.13 diopters
Posterior surface of crystalline lens, plus 9.53 diopters

These results are obtained by taking the reciprocal of the first focal length of each of these surfaces, the focal lengths being calculated from the given radii and indexes. The powers can be directly obtained by using my simplified formula: D equals aM, in which D stands for dioptric power as determined by the first focal length; a stands for the index (relative index) of the second medium less unity, and M stands for the curvature of the surface expressed in metrecs,[1] obtained by dividing the radius in millimeters into 1,000.

Using Tscherning's data for the radii (r) and indexes (n), the anterior surface of the cornea is calculated as follows: r equals 7.98 mm.; n of the cornea equals 1.377; M equals 125.3. Therefore, D equals 0.377×125.3, equals 47.24.

For the posterior surface of the cornea (the anterior surface of the aqueous), r equals 6.22 mm.; n of the cornea equals 1.377; n of the aqueous equals 1.3365; the *relative* index of the aqueous equals 0.9706, and a equals minus 0.0294; M equals 160.77. Accordingly, D equals minus 0.0294×160.77, equals minus 4.73.

For the anterior surface of the crystalline lens, r equals 10.2 mm., n of the aqueous equals 1.3365; n of the lens equals 1.42; the relative index of the lens equals 1.0625. Substituting in D equals aM, D equals 0.0625×98.04, equals 6.13. Finally, for the posterior surface of the lens (really the anterior surface of the vitreous), r equals 6.17 mm.; n of the lens equals 1.42; n of the vitreous equals 1.3365, and the relative index of the vitreous equals 0.9412. Here a equals minus 0.0588; M equals minus 162.07, and D equals plus 9.53.

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APPLYING TSCHERNING'S METHOD TO GULLSTRAND'S FIGURES

If one takes the data of the radii and indexes as given by Gullstrand and calculates the corresponding powers "according to the method of Tscherning," using my simplified formula $D = aM$, the following results are obtained: For the anterior surface of the cornea, r equals 7.7 mm.; n of the cornea equals 1.376. Substituting in D equals aM, D equals 0.376×129.87, equals 48.83. For the posterior surface of the cornea (really the anterior surface of the aqueous), r equals 6.8 mm.; n of the cornea equals 1.376; n of the aqueous equals 1.336, and the relative index of the aqueous equals 0.9709. Substituting in D equals aM, D equals minus 0.0291×147.06, equals minus 4.28. For the anterior surface of the lens, using r equals plus 10 mm. n of the lens equals 1.386 and n of the aqueous equals 1.336, one gets by similar calculation, D equals 0.0374×100, equals plus 3.74 diopters. Finally, for the posterior surface of the lens (the anterior surface of the vitreous), using Gullstrand's data, r equals minus 6 mm.; n of the lens equals 1.386; n of the vitreous equals 1.336, and the relative index of the vitreous equals 0.964. Substituting and calculating, D equals minus $0.036 \times$ minus 166.67, equals 6 diopters.

However, if one refers to the powers of these surfaces as calculated by Gullstrand, using the same data as given, for example, in Southall's "Mirrors, Prisms, and Lenses," [2] one finds different results, except for the anterior surface of cornea. The results are as follows:

	By Gullstrand's Method	By Tscherning's Method
Anterior surface of cornea.....	+ 48.83	+ 48.83
Posterior surface of cornea.....	— 5.88	— 4.28
Anterior surface of lens.....	+ 5.00	+ 3.74
Posterior surface of lens.....	+ 8.33	+ 6.00

It must be emphasized that these different results have been obtained from the same data, the data as given by Gullstrand. What is the reason for these differences?

INTRODUCING THE IDEA OF "REDUCED FOCAL LENGTH"

The reason is that Gullstrand used as a measure of dioptric, or refracting, power, not the reciprocal of the actual focal length (first focal length), but the reciprocal of the *reduced* focal length. The reduced focal length is the actual focal length divided by the corresponding index. Thus if f' and f'' represent the actual focal lengths, first and second, respectively, and n' and n'' similarly represent the two indexes, the reduced focal length, say f^r equals f' divided by n' or f'' divided by

2. Southall, J. P. C.: Mirrors, Prisms, and Lenses: A Text-Book of Geometrical Optics, New York, The Macmillan Company, 1918.

n''; therefore, but one numerical value as represented by the reduced focal length is used for expressing dioptric power.

For example, using the system of actual focal lengths for denoting power, the anterior surface of the cornea has two powers, depending on whether the anterior focal length or the posterior focal length is used. But when the system of reduced focal length is used to denote power, the anterior surface of the cornea has but *one* dioptric power, the reciprocal of the reduced focal length.

To calculate dioptric power of a surface by the reduced focal length system, one can use the same formula, D equals aM, with this difference in application. Thus, a stands for the *difference* between the two indexes of refraction as they are given. It is not necessary to find the relative index of the second medium and then subtract unity from that, but merely to subtract the first index from the second. This makes the application of the formula, D equals aM, especially easy. For example, to find the "reduced" power of the posterior surface of the cornea, one again takes the data of Gullstrand, in which r equals 6.8 mm., n' of the cornea equals 1.376 and n'' of the aqueous equals 1.336, and, using the formula in $D = aM$, a equals 1.336 less 1.376, equals minus 0.040; M equals 147.06; multiplying these gives minus 5.88 diopters (as found by Gullstrand).

For the anterior surface of the crystalline lens, one likewise uses D equals aM, in which a equals 1.386 less 1.336, equals 0.050; M equals 100; accordingly, D equals 0.050×100, equals plus 5 diopters.

For the posterior surface of the crystalline lens, a equals 1.336 minus 1.386, equals minus 0.050; M equals minus 166.67, and D equals minus $0.050 \times$ minus 166.67, equals plus 8.33.

This conception of refracting power as dependent on "reduced focal length" is helpful in many ways, and the reader is referred for a fuller discussion of this subject to Professor Southall's "Mirrors, Prisms, and Lenses."[2] It will be seen, however, from the foregoing facts that this system simplifies expression of dioptric power. There is only one power ("reduced") to a refracting surface (or a lens separating different mediums), not two powers. Only one formula need be used (D equals aM) instead of two, the foregoing one and $D = \frac{aM}{n}$ (D equals aM over n).[1] In this, a is easily obtained with less calculation and work, being merely the difference between the two indexes as they are given.

Furthermore, having found D (reduced), one can also easily get the actual focal lengths. From D one gets the "reduced focal length," and the multiplication of this by the corresponding index gives the corresponding focal length. Thus f^r equals $n' f'$ equals $n'' f''$.

For example, it was found that the power (reduced) of the anterior surface of the crystalline lens is plus 5 diopters; the reduced focal length is therefore 20 cm. The first (actual) focal length f' equals 1.336×20,

equals 26.72 cm. The second (actual) focal length f' equals 1.386×20, equals 27.72 cm. Of course, as the actual focal lengths have been obtained from the reduced focal length, one can also express the power by the actual focal lengths by merely taking the corresponding reciprocals, results conforming to those of Tscherning and most other writers being obtained.

SUMMARY

The dioptric power of a refracting surface or of any system as a whole may be expressed as the reciprocal either of the first (actual) focal length or of the second (actual) focal length. As these two are different except when the first and last mediums have the same index, two different expressions are obtained for the power of the surface. Usually the power as determined by the first (actual) focal length has been used as the standard. This method of denoting dioptric power has been the prevalent method, and is the only one used in practically all English works on the subject. A new and better method of denoting dioptric power has recently been introduced especially by continental writers. This method involves the conception of a "reduced" focal length.

By a simple mathematic relation, the two (actual) focal lengths can be resolved into a single value, the so-called reduced focal length, and the reciprocal of this value stands for the refracting power of the surface or the system. From the "reduced" focal length the two (actual) focal lengths can be easily obtained by multipying the reduced focal length by the corresponding index, i. e., by the first index to obtain the first focal length and by the second (or last) index to obtain the second focal length. The single formula D equals aM suffices for all calculations and is especially easy of application when this method of determining dioptric power is being used.

METASTATIC SARCOMA OF THE CHOROID

REPORT OF A CASE

W. E. FRY, M.D.
PHILADELPHIA

Metastatic sarcoma of the choroid is an unusual condition. Parsons,[1] in his book "The Pathology of the Eye," made the statement that there are no well authenticated cases of this condition on record. He expressed the belief that in all cases of sarcoma of the choroid it is impossible to be absolutely certain that the eye contains the primary tumor, but that the balance of evidence is in favor of this view.

In an examination of the literature, the following nine case reports have been found. The literature is discussed by Ginsberg[2] in the "Handbuch der speziellen pathologischen Anatomie und Histologie" by Henke and Lubarsch, but the condition is sufficiently unusual to allow a brief review of the reported cases at this time.

In 1870, Brömser[3] reported a case of melanotic sarcoma of the choroid that occurred a year after a pigmented nevus had been removed from the cheek of a patient by means of a ligature. Although the eye was examined microscopically, the nevus was not so examined. Schiess-Gemuseus and Roth,[4] in 1879, recorded a case history in which there was a primary pigmented nevus in the region of the sternum and in which microscopic examination of the secondary growth in the eye showed involvement of the optic nerve and adjacent tissue. In Pflüger's case,[5] which was reported in 1885, there was a pigmented nevus in the region of the right parotid gland, followed by generalized metastasis. Ophthalmoscopic examination showed an intra-ocular tumor, but no autopsy or microscopic examination was made. Parsons referred to the foregoing three cases, but rejected them as being undoubted records of metastatic sarcoma of the choroid.

Meigs and de Schweinitz,[6] in 1894, put on record a case of primary round cell sarcoma of the anterior mediastinum, in which the origin

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From the Department of Ophthalmology of the University of Pennsylvania.

1. Parsons, J. H.: The Pathology of the Eye, London, Hodder & Stoughton, Ltd., 1904.
2. Ginsberg, in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926.
3. Brömser: Inaug. Diss., Berlin, 1870.
4. Schiess-Gemuseus and Roth: Arch. f. Ophth. **25**:177, 1879.
5. Pflüger: Arch. f. Augenh. **14**:129, 1885.
6. Meigs, A. V., and de Schweinitz, G E.: Am. J. M. Sc. **108**:193, 1894.

of the new growth was believed to be in some remnant of the thymus gland. There was metastasis, which included the choroid of both eyes as well as the oculomotor and optic nerves and the extra-ocular muscles. Because the neoplastic tissue in the choroid was surrounded by comparatively healthy tissue and was not contiguous with infiltrations located elsewhere and because the blood vessels within them and in their immediate vicinity contained cells of the same character, the authors concluded that the metastatic nodules were of embolic origin.

Wiener [7] reported before the Ophthalmic Section of the American Medical Association, in 1902, a case of multiple metastatic lesions of the choroid of both eyes, in which the primary growth was in the mediastinum. The history of the patient was not complete, and there was no postmortem examination. Adamük considered the foregoing two cases to be malignant lymphomas.

The choroidal sarcoma described by Neese,[8] in 1907, accompanied a tumor of the breast. Although the cellular structure of the two growths was different, he believed that the two tumors were related and that the choroidal growth was metastatic.

In 1909, Adamük [9] recorded a case of melanosarcoma of the lid and conjunctival tissue of the left eye, in which the growth was removed by exenteration of the orbit and excision of both lids. Two and a half years later diffuse melanosarcoma of the skin developed, with symptoms of intracranial involvement and with an iridocyclitis of the remaining eye. Microscopic examination after removal of the eye revealed a melanosarcoma of the ciliary body.

The primary growth in the case recorded by ten Doesschate,[10] published in 1919, was a melanosarcoma of the right eye. The eye was enucleated. Generalized metastasis resulted, including the skin, brain and choroid of the left eye.

The most recently reported case history was in 1926, by H. H. Elschnig.[11] In this case there was a primary spindle cell sarcoma of the left ovary. There was a metastatic growth extending into the anterior chamber at the base of the iris of the right eye. An attempt was made to remove the growth by operation. Histologic examination of the removed material revealed a spindle cell sarcoma. After the death of the patient, the eye was sectioned, and a spindle cell sarcoma of the anterior portion of the ciliary body was demonstrated.

The present report concerns the following case:

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7. Wiener, Meyer: Metastatic Sarcoma of the Choroid, J. A. M. A. **39**:1158 (Nov. 8) 1902.

8. Neese: Jahresb. d. Ophth. **38**:220, 1907.

9. Adamük: Ztschr. f. Augenh. **21**:505, 1909.

10. ten Doesschate, G.: Nederl. tijdschr. v. geneesk. **2**:1432, 1919; abstr., Klin. Monatsbl. f. Augenh. **66**:766, 1921.

11. Elschnig, H. H.: Arch. f. Ophth. **117**:316, 1926.

REPORT OF A CASE

History.—F. J. S., a man, aged 49, who was admitted to the medical wards of the University Hospital on March 10, 1931, gave a history of having a pigmented mole about 2.5 cm. in diameter on the left shoulder. A year previously the mole had been injured by a falling beam. The area had scabbed over but had never healed. The patient had remained well until nine weeks previous to admission, when he became acutely ill with chill, fever and paralysis of the deltoid, biceps and supinator muscles of the hand on the right side. During the past nine weeks he

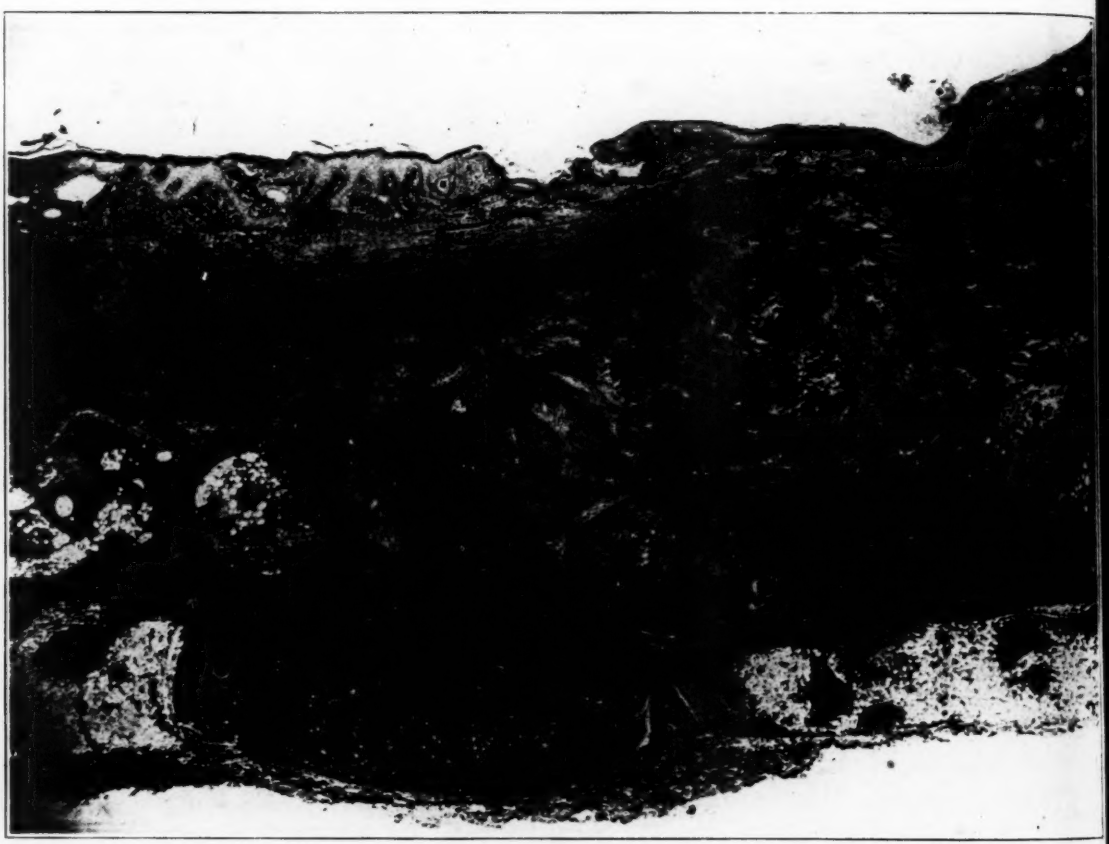


Fig. 1.—Microscopic section of the initial lesion of the skin of the left shoulder.

had lost 30 pounds (13.6 Kg.) and complained of dizziness and dyspnea. He had had no difficulty with his eyes, but required glasses for reading. He had several small pigmented nodules on his skin, one of which, about 1 cm. in diameter, had appeared at the time of his acute illness.

His previous medical history was good. He had been ill only once before, and that was with a cold that kept him in bed for three days. His family and social histories were unimportant.

Examination.—On physical examination a crusted, cornified area about 2.5 cm. in diameter was found on the left shoulder. This area was indurated and bound down to the subcutaneous tissue. There were several other pigmented as well as nonpigmented plaques. The cervical lymph nodes were enlarged. Examination

of the heart and lungs gave negative results. Both the liver and the spleen were enlarged. The Wassermann reaction of the blood was negative.

An ocular examination was made by Dr. Cowan. There was a small pigmented area under the conjunctiva of the left eye, about 10 mm. above the limbus. The fundus examination of the right eye showed that the media were clear, and the disk was yellowish and had well defined outlines. There was a large physiologic cup; the arteries were normal, and no lesions were seen. The fundus of the left eye

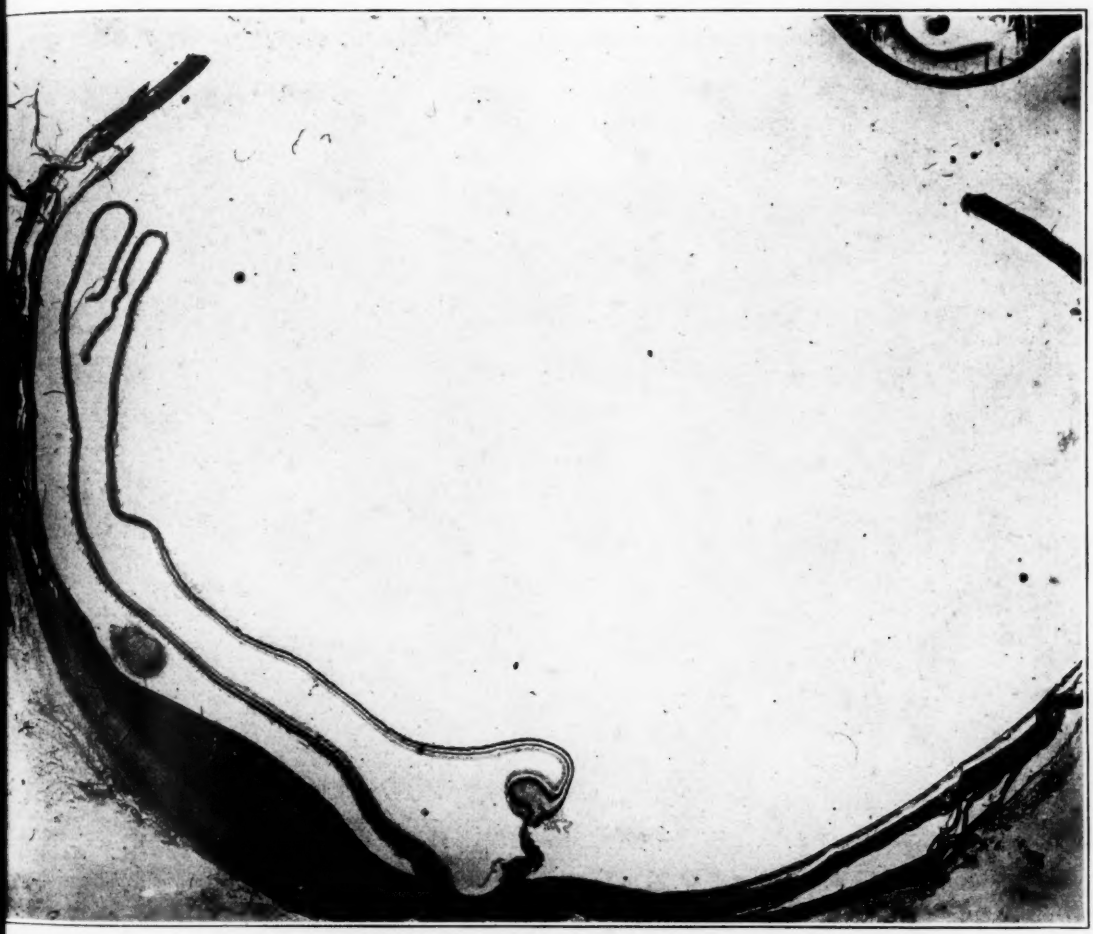


Fig. 2.—Section of the posterior portion of the left eye, showing the growth adjacent to the disk.

was similar, except that just to the temporal side of the disk there was an area about 1.5 disk diameters in size, which was yellowish and surrounded with pigment.

The patient rapidly became worse and died six days after the date of admission.

Autopsy.—A complete autopsy was performed, and malignant melanomas were found in the following organs: skin, thyroid, heart, lungs, liver, spleen, pancreas, suprarenals, kidneys, bladder and prostate, gastro-intestinal tract, lymph nodes, bone marrow, skull, brain, aorta and choroid of the left eye.

Since the present report concerns the metastatic tumors of the choroid, the pathologic description will be limited to the primary lesion in the skin of the shoulder and the metastatic lesions of the choroid of the left eye.

Dr. Klink, of the department of pathology, gave the following description of the primary lesion. The keratinous layer of the skin was absent from part of the center of the section. In this region the papillae were either absent or poorly formed. On either side of this area the papillae tended to become normal in appearance. At one end of the section relatively normal skin was found. The entire section was pervaded by a neoplasm that consisted of epithelium-like cells having an indefinite cellular outline and large vesicular, deeply staining nuclei.

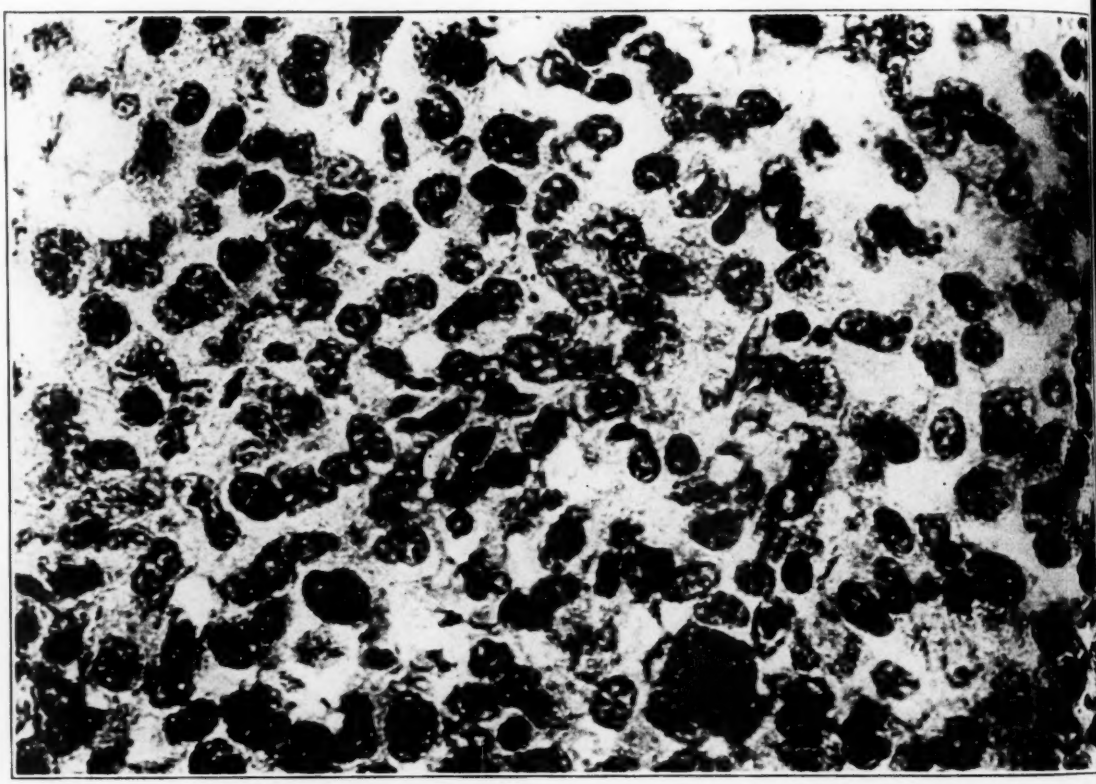


Fig. 3.—Higher magnification of the cells of the growth adjacent to the disk in the left eye.

In some portions the tumor appeared to carry with it some fibrous stroma, but this was probably the original stroma of the subcutaneous tissue. Associated with the tumor cells were a few that contained and were surrounded by brown granular pigment. The amount of pigment was unusually small when the deep pigmentation of the gross specimen was recalled. The entire subcutaneous tissue was pervaded by neoplasm and remnants of muscle, blood vessels, sweat ducts and fat cells, which were surrounded and invaded by tumor cells.

At the time of autopsy, which was performed one hour after death, the posterior half of the left globe with 7 mm. of the optic nerve was removed, and microscopic sections were prepared. Gross examination of the cut specimen showed, adjacent to the optic nerve, a flat growth of the choroid, measuring 7 by 1 mm. To either

side of the growth there was a small amount of hemorrhage. Microscopic examination of the specimen revealed the growth to be a well circumscribed tumor of the choroid, consisting of round cells and a sparse amount of pigment. The retinal pigment epithelium was intact over the growth, and there was no involvement of the sclera. The cells were predominately of the round cell type and of varying size, many of the cells being of the large round cell type. The nuclei stained well with hematoxylin. No spindle or elongated cells were seen, except those which formed the lining wall of the capillaries. There were a number of areas of small hemorrhages within the tumor. At the site of the growth none of the layers of the choroid could be identified. In addition to the larger growth, the choroid contained several smaller growths. One section contained four of these additional growths. These growths consisted of the same type of round cell, and the area

Fig. 4.—Portion of the choroid of the left eye, with tumor cells within a choroidal vessel.

containing them was well circumscribed. In one instance the tumor cells were contained within the walls of a choroidal capillary.

The retina was detached in the course of the preparation. All the retinal layers were intact, but there was degeneration in the layer of rods and cones and in the ganglion cells. There were no tumor cells or hemorrhages seen within the retinal layers.

The section of the papilla did not show a pathologic cupping, and there were no tumor cells within the optic nerve or contained within its sheaths.

The cells composing the tumors of the choroid were of the same type and had the same staining characteristics as the cells of the pigmented nevus of the shoulder.

COMMENT

Since primary sarcoma of the choroid with generalized metastasis is the usual condition and primary sarcoma elsewhere, with secondary

sarcoma of the choroid, is the rare condition, the reasons for presenting a case representative of the latter type should be scrutinized.

In the present instance there was a definite history of a pigmented nevus of long standing that was injured and did not heal, and also there was the lack of any symptoms of ocular difficulty. Microscopic examination of the lesion of the skin showed the growth of the cells to be irregular and infiltrating, as would be expected in a primary tumor, while the lesions of the choroid were well circumscribed, as would be anticipated in a secondary tumor. The cells in both instances were the same in size and staining characteristics. It would be unlikely for metastasis to occur in an already existing pigmented nevus, which would be the supposition if the lesion in the eye was considered primary. That intra-ocular metastasis from a pigmented nevus that has undergone malignant changes is possible is demonstrated by the case of Schiess-Gemuseus and Roth, in which the intra-ocular tumor in the nerve head occupied a position entirely out of keeping with the view that the ocular growth could be a primary choroidal sarcoma. The fact that there were several nodules in the eye sufficiently separated to rule out a continuity of growth adds more evidence for believing that the choroidal growths are secondary. At one point the tumor cells were seen within the lumen of a choroidal vessel. Metastasis within the choroid is rarely found. The location of the largest lesion of the choroid was such, and the size sufficient, as to encroach on the macular region. This would give enough interference with the vision of the patient for him to be conscious of his ocular difficulty, had the condition existed for a long period previous to his death. Although no one of the foregoing reasons is sufficient to make the present case an instance of metastatic sarcoma of the choroid, when they are all considered, I believe, it is justifiable to classify the ocular condition as undoubtedly secondary.

ABSTRACT OF DISCUSSION

Dr. George E. de Schweinitz: It is well known that Hofrat Fuchs, in his famous monograph "Das Sarcom des uveal Tractus," stated that metastatic choroidal sarcoma was unknown, and that he (Fuchs) had quoted Virchow's sentence: "Those organs which exhibit a great tendency to protopathic tumor formation present a very slight inclination to metastatic deposits." Similar views were held by Professor Axenfeld, and are recorded by some of the English observers, for instance, Sir John Parsons. And yet it is true that such metastases apparently do take place, as in the case studied by the late Dr. A. V. Meigs and myself in 1894, and in the patient referred to by the essayist.

The original growth in the case studied by Dr. Meigs and myself, in an Italian, aged 21, was situated in the anterior mediastinum and proved to be a round cell sarcoma, which was the cause of the death of the patient. Sarcomatous deposits were found in many organs and tissues—the lungs, liver, spleen, kidneys, etc.—and this extensive metastasis included the brain, both choroid coats, the oculomotor and optic nerves and the exterior ocular muscles.

The deposits of sarcoma cells in each choroid, but particularly in that of the left eye, give this case an importance in the literature pertaining to sarcoma of the uveal tract. The facts that these deposits were limited to a certain area of the choroid, that they were surrounded by comparatively healthy tissue not contiguous with infiltrations located elsewhere and that the blood vessels within them and in their immediate vicinity contained cells of the same character afforded evidence that they should be regarded as metastatic nodules. Moreover, the deposits were bilateral, while primary sarcoma of the choroid is always unilateral.

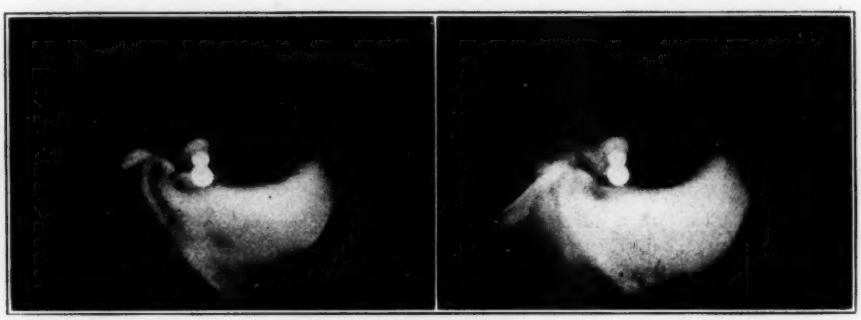
DR. LUTHER C. PETER: Because of the infrequency of the occurrence of metastasis of sarcoma into the choroid, I wish to record a case which occurred in the Graduate Hospital about two years ago. The primary growth was in the skin of the upper arm. Metastases were multiple, and the eye was invaded only during the last two weeks of the patient's life. During this time it was interesting to note the rapid development of the pathologic changes within the right eye. In this instance, the changes in the eye were definitely secondary and not primary. Complete pathologic studies were made. The same type of cell was found in each lesion, including that in the choroid, and the pathologists and clinicians agreed in the diagnosis of secondary invasion of the choroid, the primary lesion being in the upper part of the arm.

Clinical Notes

UNUSUAL TYPE OF DETACHMENT OF THE RETINA

MICHAEL GOLDENBURG, M.D., CHICAGO

Detachment of the retina ordinarily presents no problem in its diagnosis to the average clinician. Occasionally it is difficult to state whether the detachment is due to an accumulation of fluid posterior to the retina or whether the retina is pushed forward by a neoplasm. In the cases to be reported, virtually all of the classic diagnostic features were absent, and it was some time before a definite diagnosis could be offered and a theory advanced to account for the picture presented. Even then the diagnosis was not concurred in, although the theoretical explanation offered was conceded to be attractive. It was not until about eight months after the first patient was seen, when a patient with an exact duplicate of the case appeared and was hospitalized for study, during which spontaneous reattachment took place, that the diagnosis was definitely confirmed.



The fundus in case 1. Note the faint line in the fold of the detached part of the retina, running outward and downward, probably the posterior aspect of the upper temporal branch of the central retinal artery. The fold in the retina running down and nasalward probably indicates the nasal branch of the artery. Note the outline of the upper margin of the disk and the absence of blood vessels in the upper field. Photograph by Von Der Heydt.

As a result of this study, several interesting features other than the retinal detachment were manifested in such a manner as to make the cases of more than ordinary interest. The controversy concerning the hyaloid membrane would appear to be brought into such light that its presence or absence should be settled. Likewise, the classic anatomic structure of the vitreous may be seriously questioned.

REPORT OF CASES

CASE 1.—R. M.,[1] aged 32, a teamster, presented himself at the clinic on Feb. 23, 1931, with the following history: About six months previously he was

From the Eye Department of the Illinois Charitable Eye and Ear Infirmary.

1. This case was presented at a clinical meeting of the staff of the Illinois Eye and Ear Infirmary, March 11, 1931.

struck in the left eye by the fist of an opponent. He noticed soon after this accident that the vision in this eye was poor, but thought little of it at the time, attributing the visual disturbance to the swollen black eyelids which he could not open. However, when the eyelids and redness of the eyeball returned to normal and the vision remained poor, he became alarmed and appeared at the clinic. External examination disclosed no evidence of injury in either eye.

Fundus Examination Under a Mydriatic—The right fundus was normal in every respect.

The upper part of the media of the left fundus was clear, and in the lower part a grayish area was noted.

The nerve head could not be located. In the upper three fifths of the field the typical stippled orange-pink background was clearly visible with a total absence of blood vessels in this region. At about where the upper level of the nerve head should be, one could make out what appeared like a folded grayish-white layer of tissue that extended downward as far as one could see, covering everything in the lower part of the field. In the upper central part of this fold a tear was seen, and along the temporal edge of this tear a tortuous bluish-red streak about the diameter of a blood vessel could be made out.

After some study the diagnosis of detachment of the retina was ventured on the following basis: the previous history of good vision in both eyes, trauma and, immediately following the injury of one eye, the loss of vision in that eye. The absence of blood vessels in the upper field and the absence of any evidence of edema or inflammation in the presence of a perfectly normal and clearly visible background could be explained only on the basis of total detachment of the retina in this region, the tear taking place probably in the region of the ora serrata, the retina falling down so as to cover the nerve head and everything below it, leaving the pigment epithelial layer intact and in a normal position, thus giving to this region its normal coloring. The bluish-red streak seen in the grayish membrane below must therefore have been a retinal blood vessel seen from its posterior aspect through the layers of the detached retina. The patient was hospitalized for the purpose of further study. He was put to bed and remained on his back for several weeks; he was given the attention that seemed indicated, but without improvement. My associates and I could devise no definite procedure to follow in a case of this type. In the latter part of the patient's stay in the hospital, through a widely dilated pupil one could make out some normal vessels below in the extreme periphery, beyond the edge of the detached fold of the retina. These vessels, it was concluded, belonged to the normal part of the retina that had not been detached.

In case 2 a similar picture and history were presented, with the added unusual phenomenon of spontaneous reattachment and later relapse, proving beyond question the diagnosis in these cases.

CASE 2.—Jos. C.,[2] aged 22, a laborer and amateur boxer, presented himself on Oct. 29, 1931, with the history that while boxing about three weeks previously he had received a blow in the right eye but, he paid no particular attention to it. About one week later he noticed that his vision in the lower part of the field was

2. This case was presented before the Chicago Ophthalmological Society, April 18, 1932.

dark. Then for several days the vision varied from complete blindness to almost perfect vision in this eye.

Examination disclosed a pupillary reaction to light; accommodation and the consensual reaction were good.

Vision in the right eye was limited to light perception; that in the left eye was 20/10.

The physical and laboratory findings were negative.

Ophthalmoscopic examination disclosed a duplicate of the picture presented in case 1, with slight but unimportant differences. The young man was hospitalized for the purpose of study and observation. As the case was similar to case 1, no attempt was made to place the patient at rest in the hope of reattachment, as this had been tried in the previous case with no benefit. His right pupil was kept dilated with atropine sulphate, so that he could be examined at any time, and he was permitted to do orderly work around the hospital. A few days after his admission he reported to the intern that he could again see with that eye. The intern immediately used the ophthalmoscope, and reported that reattachment had taken place, which was confirmed the following day. In the extreme periphery of the upper field one could easily see a long horizontal tear in the retina parallel with the ora serrata; the edges of the torn retina were irregular, with the tendency for the edges to curl toward the vitreous. The patient was put to bed at once and kept in the recumbent position. A few days later he reported that his vision was gone again, and examination disclosed the retina again detached as on the day of his admission to the hospital. It had remained so ever since.

COMMENT

The interesting features in these two cases, other than the unusual and I think rare type of detachment of the retina, are: (1) the ability of the retina to float down over the nerve head without any evidence of disturbance of the vitreous; (2) spontaneous reattachment with a return of function while the patient was doing orderly work around the hospital; the only medication resorted to was the instillation of atropine sulphate; (3) the perfectly normal coloring of the upper field, indicating the cleancut separation of the pigment epithelial layer from the layers of the retina anterior to it and the definite proof that to this layer must be attributed the normal coloring of the fundus; (4) the controversy concerning the hyaloid membrane would appear to have much light thrown on it in these cases.

If this membrane actually does exist, how is it possible for the retina to be carried downward through this membrane and through the vitreous as though it were an aqueous solution? The detached retina not only covered the optic nerve so it could not be seen, but covered the lower field so completely that the vessels in this region could be seen only in the extreme periphery, and later it reattached itself spontaneously. This occurred in case 2 without disclosing any changes in the vitreous or the so-called hyaloid membrane. This case would also seem to question the actual consistency of the vitreous in vivo; also it would appear to prove Duke-Elder's deduction that the so-called framework of the vitreous which can be seen with the slit-lamp is an optical illusion and does not exist, or it could not permit the detached part of the retina to float down so freely.

104 South Michigan Avenue.

PROGRESSIVE REFRACTION CHANGES FOLLOWING TREPHINE OPERATION

JAMES W. SMITH, M.D., NEW YORK

Sclerocorneal trephine as popularized by Elliot has been accepted as the classic surgical aid in chronic noninflammatory glaucoma. Unfortunately most patients seek relief only when the perimetric field is seriously impaired, and too often poor vision after operation is ascribed to the trephine operation. Certain complications and sequelae may occur. Colonel Elliot [1] has recently published an excellent paper outlining precautions necessary to insure more uniform postoperative results. No mention is made by him of permanent refraction changes after operation, and Zentmayer,[2] in reporting five cases of marked differences in refraction after operation, stressed the phenomenon, which is rarely referred to in the literature.

The patient described in this presentation required eleven corrections of the lens, varying from moderately high hyperopia to moderately high myopia.

REPORT OF A CASE

L. W., a woman, aged 56 at the time of the first examination on Dec. 5, 1927, complained of cloudy vision in the left eye for the preceding six months. Corrected vision in the right eye was 15/20 plus; that in the left eye, 15/20. Intra-ocular tension, measured with the Schiötz tonometer, was 30 in the right eye and 35 in the left eye. The anterior chambers were slightly shallow, and both optic nerves showed glaucomatous excavation, more marked in the left eye. The right field of vision was normal, and the left showed a sector loss superiorly and nasally. Treatment with miotics was instituted, with a reduction of tension to normal and an improvement in vision to 15/15 in both eyes. After one month the tension in the left eye again increased, and on Jan. 9, 1928, an Elliot trephine operation was performed on the left eye at the Post-Graduate Hospital. The trephine button was forced into the anterior chamber, and no bulge of the iris followed the operation. A small section of peripheral iris was excised, and there was a possibility that the ciliary body had been slightly traumatized. The patient made an uneventful recovery, and during the past four and one-half years the intra-ocular pressure had averaged 18 mm. of mercury.

At the time of operation the patient was wearing a hyperopic correction, O.D. 2.50 sph. $= 0.50 \times 180$, O.S. 2.75 sph. $= 0.25 \times 75$. Six weeks after the operation a new prescription was ordered for the left eye, reducing the hyperopia by 1.5 diopters. One month later it was necessary to return to the preoperative prescription for improvement in vision to 15/15 minus. Two months later it was necessary to increase the hyperopic correction 0.75 diopter. Following this prescription a gradual and progressive decrease in the hyperopia developed, so that it was neces-

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Read before the Section of Ophthalmology, New York Academy of Medicine, May 16, 1932.

1. Elliot, R. H.: Some Afterthoughts on Trephining for Glaucoma, Am. J. Ophth. **14**:999 (Oct.) 1931.

2. Zentmayer, W.: Sclerocorneal Trephining in Chronic Simple Glaucoma, Am. J. Ophth. **14**:617 (July) 1931.

sary in the following year to eliminate all of the hyperopic acceptance, and in June, 1930, the patient was given minus glasses. During the past eighteen months it had been necessary to increase the minus correction four times. Since the operation, three and one-half years previously, eleven different prescriptions had been ordered for the left eye. It is interesting to note that with the first six pairs of hyperopic glasses, the last of which was ordered on March 25, 1930, it was possible to improve the acuity to 15/15. Since June, 1930, with myopic lenses, there had been no improvement in vision possible beyond 15/30 minus. The field of vision in the left eye, which was examined repeatedly, remained unchanged until four months prior to this presentation, when a further loss in the field supertemporally was noted.

Slit-lamp examination of the dilated left pupil revealed atrophy of the iris stroma at the pupillary edge and remains of a low grade exudate, which was first noted on Oct. 28, 1930. On the anterior capsule of the lens was seen pigment

Refractions and Visual Acuity

12/ 5/27	Correction at time of first examination Plus 2.50 sph. 0.50 cyl. × 180 = 15/20 + Plus 2.75 sph. 0.25 cyl. × 75 = 15/20 —		
1/ 9/28	Sclerocorneal trephining of left eye		
Corrected acuity O.S.		Prescription ordered	
2/15/28	15/40 —	Hyperopic	1.50 sph. 0.50 cyl. × 60 = 15/20 + 2
4/12/28	15/50 —		2.75 sph. 0.50 cyl. × 60 = 15/15 —
6/19/28	15/50		3.50 sph. 0.50 cyl. × 60 = 15/15 — 2
6/ 6/29	15/40 +		2.50 sph. 0.50 cyl. × 60 = 15/15 —
10/31/29	15/40 +		No prescription ordered
12/17/29	15/100		1.00 sph. 0.50 cyl. × 60 = 15/15 —
3/25/30	15/40 —		
5/ 6/30	15/70		0.50 sph. 0.50 cyl. × 60 = 15/15
6/17/30	15/30		
8/ 5/30	15/70	Myopic	0.50 sph. 0.25 cyl. × 120 = 15/30
9/23/30	15/70		
10/28/30	15/100		—1.00 sph. —0.75 cyl. × 120 = 15/30 +
1/ 6/31	15/100 —		—1.50 sph. —0.50 cyl. × 120 = 15/30 +
5/12/30	15/50 —		
12/17/31	15/100 —		—2.75 sph. —0.75 cyl. × 150 = 15/50 (Refracted out of town)
5/12/32	15/70		—3.25 sph. = 15/30 —

Average intra-ocular pressure 18 mm. of mercury (Schiötz)

débris which blurred the view of the fundus. No vitreous opacities were seen, and the optic nerve appeared excavated 6 diopters. The patient had at no time since the operation had any marked discomfort in the left eye. Six months before this article was written some nuclear sclerosis of the lens was noted. A tentative diagnosis of quiet iritis was made, either following retention of a scleral plug in the angle of the anterior chamber or possibly due to slight injury of the ciliary body at the time of the trephine.

COMMENT

In the four years following sclerocorneal trephining 6.5 diopters of myopia developed. For two and a half years after operation the acuity with proper lenses could be corrected to normal, and reduction in the perimetric field had occurred only during the past four months. It was at first believed that the marked changes in refraction might be due to alterations in the rate of filtration, bringing about a change in the curvature of the lens, but Cowan [3] considered the difference in refraction too great to be thus accounted for.

3. Cowan, cited by Zentmayer.[2]

Colonel Elliot [4] considered three conditions in which alterations in refraction are found after trephining:

1. Myopia due to an advance in the lenticular system, resulting in free emptying of the anterior chamber.

2. An occasional change of latent hyperopia into manifest hyperopia, following prolonged use of atropine after operation.

3. Increasing myopia due to sclerosis of the lens.

Sclerosis of the lens is often found apart from glaucoma, and it is difficult to state whether there is a direct association between the two conditions. Elliot has not been able to explain such changes in the lens as due to faulty technic in the operation. There is also the possibility that the so-called quiet iritis may prejudicially influence the nutrition of the lens.

According to Zentmayer,[3] permanent changes in refraction following sclerocorneal trephining are of sufficient importance and frequency to warrant mention in textbooks on ophthalmology.

ABSTRACT OF DISCUSSION

DR. S. A. AGATSTON: Recently I saw a patient who had low grade iridocyclitis. On my first examination of this patient, which was several months ago, there was hypermetropia of 3 diopters. At the last examination, she showed myopia of 2 diopters; I could not explain the cause. There was no nuclear sclerosis.

DR. HERBERT W. WOOTTON: I have seen several cases of progressive contraction of the visual fields after trephining, although the central vision remained practically normal, and the tension always remained well under normal limits.

4. Personal communication to the author.

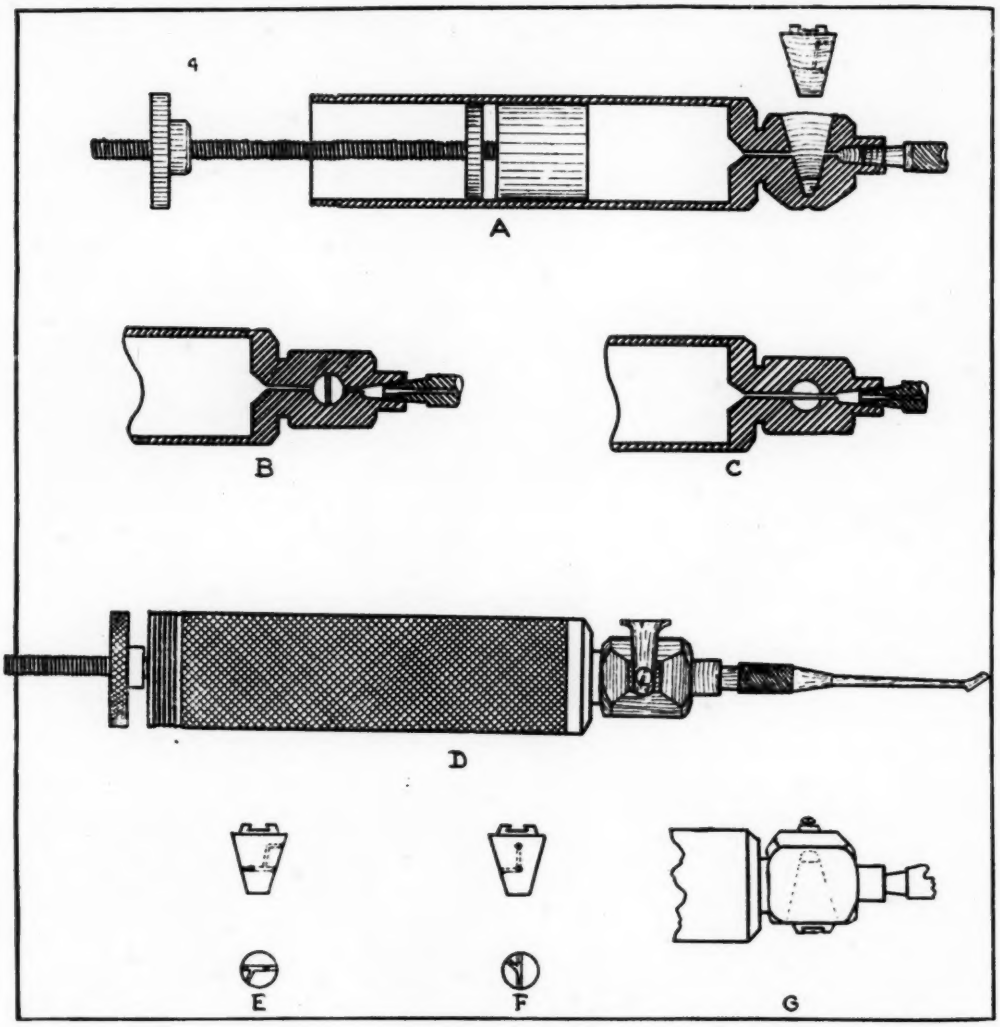
A VACUUM GRASPING INSTRUMENT FOR REMOVAL OF CATARACT IN CAPSULE

THEODORE J. DIMITRY, M.D., NEW ORLEANS

This article describes an instrument that I made and have used for some years in the extraction of the cataract in its capsule. I submit it to my confrères and to the surgical instrument artisan in the hope that some one may accept the lead I offer and mechanically perfect it, so that it may be put at the disposal of many ophthalmic surgeons.

My primary object is to contrive a compact and effective device for the grasping of the lens in the capsule, so as to do away with the objectionable rubber tubing and the large vacuum container of the Barraquer, Down or Van Hulen equipment, and to bring forward a mechanism to accomplish this aim and yet to grasp and perform in a satisfactory manner so as to remove the lens in its capsule.

The instrument embodies a cylinder in which a plunger operates to produce a vacuum and to which a hollow grasping stem is connected. Between the cylinder and the stem is a valve by means of which communication between the cylinder and the grasping stem may be established or cut off; this valve may be used to release the vacuum from the stem, and yet permits a vacuum to remain in the cylinder.



Dimitry vacuum grasper.

I am of the opinion that it is simple so far as it is free from complexity or intricacy, and that it applies and controls the physical laws of vacuums in conformity with the purpose for which they are used; consequently, the whole device need not be much greater in size than a large fountain pen.

D in the accompanying figure is a perspective view of the instrument, showing the cylinder, the valve and the stem. *A* is a section taken

centrally and longitudinally through *D*. *B* and *C* show how the communication between the cylinder and the stem is made by the action of the valve, *E*, *F* and *G*.

In *A* the space between the larger and smaller plunger is filled with an extra heavy cup grease.

The instrument is comparatively small and consequently has a limited vacuum chamber, yet it has been made to perform successfully. It can be reduced still further, and in my opinion will perform equally as well, for a large volume vacuum space is not necessary to obtain a most satisfactory vacuum grasp, and if it is machined to perfection, its simplicity and ease of manipulation are calculated to give it recognition and trial.

The method of use is first to make certain that the valve is closed, which is the case when the valve is half way between its forward and backward extent of movement. To produce the vacuum the plunger is then pulled out, and in the extended position is ready for use. With the stem well attached, it is inserted through the incision into the eye, and the operator decides on the area of the lens with which he intends to make contact, and after this is accomplished the valve is opened by pushing the valve handle forward, which thereby permits communication between the valve, stem and cylinder chamber. The vacuum grasp may be released by pushing the handle backward, and in so doing the vacuum in the cylinder is not lost, because the movement of the valve opens a small hole in the valve which communicates with the stem but not with the cylinder.

In conclusion, I submit a simple vacuum grasping instrument which applies physical laws, and if the removal of the lens by vacuum grasping devices is to continue, my device, when properly machined, may prove an adaptable and acceptable instrument.

Ophthalmologic Review

EDITED BY DR. FRANCIS HEED ADLER

ETIOLOGY OF MYOPIA

FRANK H. RODIN, M.D.
SAN FRANCISCO

The essence of myopia is that parallel rays come to a focus in front of the retina. The type of myopia that will be considered is that known as axial myopia, the main cause of which is an elongation of the axis of the eye. The elongation is caused by distention of the sclera, which is bulged out posteriorly.

The cause of myopia has puzzled ophthalmologists since the condition was recognized. There are a bewilderment of opinion and a variety of conclusions. It is not my intention to review all the theories offered to explain myopia. I shall mention only those proposed recently and which seem to have some basis.

It was Johanness Kepler who in 1604 defined the science of refraction by means of convex and concave glasses as well as by the eye, and especially as regards myopia.

As early as 1644 a Chinese ophthalmologist (Pi) proposed a theory that myopia is due to mental and physical overactivity.

In 1708, Boerhaave held that myopia is due to the excessive length of the eye, and he also attributed it to the greater convexity of the cornea. Morgagni demonstrated anatomically the greater length of the myopic eye.

Donders, in 1864, attributed myopia to the tension of the eye for near objects. He held that the predisposition is almost invariably congenital and, moreover, nearly always hereditary. A consideration of all the facts led Donders to believe that fundamentally emmetropic eyes seldom, and hypermetropic eyes perhaps never, become myopic, but that, having once occurred, the myopia is often transmitted as a predisposition in posterity, and under fresh exciting causes is developed to its higher degrees. Thus, the hereditary principle accumulates in the posterity the effect of the causes repeated in every generation. In some families the myopia therefore attains a high degree, and the danger is greater, because, according to experience, the hereditary tendency manifests itself the more certainly the more the myopia has

From the Bureau of Child Hygiene, San Francisco Department of Public Health; J. C. Geiger, M.D., Director of Public Health.

already been transmitted through a number of generations and has assumed a typical character.

The causes mentioned in the modern theories of myopia can be roughly divided into mechanical, hereditary and acquired.

MECHANICAL CAUSES

The most satisfactory proof would be an experimental one. It is not necessary for me to mention the difficulty encountered in experimental ophthalmology on animals. Myopia from its very nature does not lend itself easily to such experimentation.

Levinsohn (1913), the most emphatic proponent of the mechanical theory of myopia, claimed that the force of gravity is the important cause. When a person stoops down, a certain amount of proptosis takes place; this is caused partly by the weight of the eyeball and partly by an increase of blood volume in the orbital veins. This falling forward of the eyeball causes a pull on the optic nerve and pressure by the orbital fat on the posterior pole of the eyeball. These two factors weaken the sclera at the posterior pole and cause traction on the nerve head upward and inward, which in turn gives rise to the characteristic crescents. Levinsohn produced myopia experimentally by placing monkeys so that they were compelled to look constantly downward and determined the refraction by retinoscopy. He noticed a marked increase in the refraction, amounting to 7 diopters in one case in a course of seven months.

Recently, Essed and Soewarno have repeated Levinsohn's experiment and confirmed his findings. The eyes were examined histologically by Levinsohn (1929), who found myopic crescents.

Marchesani repeated Levinsohn's experiments on myopia in apes and reported his conclusions after an observation of two and one-half years. He used fourteen animals, some of which he used as controls. In the early stages of his experiments he noticed that in some of the apes progressive myopia developed. During the same period a number of control animals also showed the same changes. Later the control animals were used in the experiment. From the experiments it was noted that some of the animals showed no apparent change in refraction, while in others myopia developed. Whether or not the animal was used in the experiment made no apparent difference. In one ape the myopia progressed while the animal was under the experiment, but ceased when the ape was set free. In another, the reverse process was present. Because of the frequency of spontaneous myopia in apes, Marchesani expressed the opinion that it is difficult to draw any definite conclusions.

Schoute, in discussing Levinsohn's theory, expressed the belief that the important factor is the optic nerve. He claimed that the length of the optic nerve varies greatly. If the optic nerve is long, the forward movement of the eyeball will be accomplished without tension on the globe. If the optic nerve is short, the posterior portion of the globe is prevented from going forward, and this tension may be a factor in the production of myopia.

Comberg, in answering Levinsohn's theory, stated that in numerous examinations of corpses there was never found in the bending optic nerve a smaller gain in length than 5 mm., and numerous exact measurements of the position of the eyeball in the orbit show with complete certainty that the eyeball extends forward from 1 to 1.5 mm. in patients lying down. In those who are sitting up, it extends no more than 0.5 mm., and the bending forward of the head has no influence at all. Hence, the eyeball cannot hang on the optic nerve, as Levinsohn claimed. Different results in experiments with monkeys can be explained by the different anatomy of a monkey and its entirely unnatural position of holding the head.

Hanssen, who had made many observations, printed a photograph of a postmortem finding which showed the enlarged optic nerve stretched backward in the shape of an S. He expressed the belief that not only does the optic nerve exercise no traction on the posterior pole, but the enlarged eyeball presses the nerve backward.

Ochi experimented on young rabbits by inserting small foreign bodies beneath the recti muscles, with a view of producing continuous pressure on the eyeball, to discover what influence, if any, such pressure might have on the diameter of the globe. No marked changes were found. He next subjected the anteroposterior diameter to stronger compressions by binding the equator of the eyeball of the young rabbits with silk threads instead of wedging in a foreign body, but there was no conclusive evidence that this caused myopia. As a result of these experiments he concluded that even fairly strong compression on the eyeball cannot greatly lengthen its diameter. Therefore, it seems likely that the pressure of the ocular muscles alone on the wall of the globe cannot greatly change the anteroposterior diameter, if the wall is normally strong. But if the resistance of the sclera is weaker than normal, even the compression of the ocular muscles alone could lengthen the anteroposterior diameter. To this pressure on the weakened sclera he ascribed the development of juvenile progressive myopia.

From the study of the structure and development of the sclera, Ochi suggested that the sclera is to be regarded as a part of the cranium. Such correspondence may serve to explain why some scrofulous, weak children may have a predisposition to progressive myopia.

Edridge-Green approached the subject from the point of view of hydrodynamics. According to him, the primary and essential cause of myopia is an obstruction to the outflow of lymph spaces between the retina and the choroid into the lymph spaces of the optic nerve. The increased ocular tension thus caused distends the sclerotic posteriorly, where it is the weakest, causing elongation of the eyeball. He further maintained that the condition most likely to give rise to myopia in subjects predisposed to it is not convergence of the eyes during near work, but unduly severe muscular effort.

The main criticism to this theory is: Is there a lymph space between the retina and choroid, and if there is, would not distention of the lymph space produce detachment of the retina long before it had any effect on the sclera, and if myopia is caused by an increase of the intraocular tension, why do myopic eyes present no symptoms of glaucoma?

Müller attributed the stretching of the posterior sclera in myopia to traction by the inferior oblique muscle. He had therefore tenotomized this muscle in twenty-five eyes of twenty-one patients, and the benefits derived from the operation, as given in his rather broad statements, include a decided lessening of high myopia, retrogression of the choroidal and retinal changes at the posterior pole and improvement of the visual acuity.

Holm (1925) advanced the theory that there exists an interrelation between the activity of the ciliary muscle and the growth of the eyeball; that the ciliary tonus furnishes a stimulation to such growths, and that an overuse of the ciliary muscle by much near work causes an overgrowth of the eyeball (i. e., an abnormal length of the anteroposterior axis) and hence myopia.

The theory is based on the following considerations: In babyhood, in a normal child, there is a marked hypermetropia due to shortness of the eyeball; as the child begins to use his eyes, the hypermetropia is overcome by the ciliary effort. This marked ciliary tonus stimulates a corresponding growth of the eyeball. Before adult life is reached the eyeball is emmetropic; by this time the ciliary tonus is lessened, and the balance of the two factors is reached. It is well known that myopia is many times more frequent among young children who do much near work than among those who do not. The myopia in the former is due to an overgrowth in the eyeball produced by an abnormal or unusual ciliary effort from the prolonged use of accommodation. The reason why myopia is less among watchmakers than among printers is, according to Holm (1926), that the former use a magnifying glass for their close work and thus are saved the strain of accommodation.

Donders stated that the reason why watchmakers, although they sit the whole day with a magnifying glass in one eye, do not develop

myopia is because they fix their work only with one eye and therefore converge but little, and because they usually avoid a stooping position.

Holm also suggested that heredity plays a part in the production of myopia.

HEREDITARY FACTORS

Incze, after careful analysis of the literature, claimed that close work plays little if any part in the development of myopia. According to him, myopia is inheritable, and the sclera is the site of alteration. He expressed the opinion that there is a certain asthenic tendency in myopia. He regarded the damage to the elastic tissue of the sclera in myopia as an expression of generalized weakness of the similar mesenchyme-derived tissue throughout the body. The eyeball is elongated by virtue of a daily fluctuating hypertonia of the intra-ocular fluids on the weakened scleral tissue.

Wood held that it is due to a hereditary defect of the ciliary muscle. This muscle consists of two parts: the outer meridional, Brücke's muscle, and the inner circular, Müller's muscle. In the latter muscle the fibers are not properly developed in myopic eyes, and it is due to this defect that Wood ascribed the causation of myopia. This lack of development is ordinarily ascribed to the lack of the use of the muscle in myopia, but the author quoted from several observers, showing that the defect is present at birth; hence, it cannot be a consequence of want of use.

Vogt held the opinion that there is no such thing as school myopia, and he drew a parallel between degeneration of myopic and senile eyes. In his opinion, both conditions are hereditary.

Clausen maintained the view of the hereditary origin of myopia. The three hundred cases of myopia of all degrees that he studied showed, in the majority of instances, a history of the same anomaly among various generations of the same family. He expressed the belief that the conception of school or work myopia should be dropped.

When experimental work is not available, a statistical study may occasionally give information that will throw light on an obscure problem. Such has been the study of Sourasky of London. He undertook a study among Jewish and non-Jewish children in the east end of London in regard to the relation of race, sex and environment in the development of myopia. The Jewish children studied were all born in England. In the vast majority of cases their parents were of Russian and Polish origin. The Jewish children were brought up in much the same way as the children of non-Jewish population, except that the boys who attended the elementary day school also attended classes for the study of Hebrew several evenings each week under

conditions that were by no means ideal. He gave the following summary of his observations:

1. The incidence of visual defects among the Jewish boys in the east end was more than 40 per cent, almost double that among the non-Jewish boys.

2. This heavy incidence of defects among Jewish boys was stationary all through their school life; it was practically no heavier at the age of 14 than at 7.

3. The incidence of the defects, therefore, was not increased with school life, and apparently was not produced by the excessive amount of work done by the Jewish boys.

4. Comparative analysis of the refractive errors seen among the defectives of the Jewish and non-Jewish children revealed little difference in the distribution of the error, apart from a rather higher incidence of myopia and of a low hyperopia among Jewish children.

5. There was little difference in the percentage of cases of myopia in the early years of school life (from 5 to 9) in the two groups. The greater incidence of myopia among Jewish children became marked in the later years (from 10 to 14).

6. It was argued that the greater increase of myopia in the later years among Jewish children was not the result of excessive close work, but of the greater incidence of low hyperopia among Jewish children.

7. When the analyses were carried further to bring out any distinction in the number of cases of myopia among Jewish boys as compared with that among girls, it was found that the increase was decidedly greater among the boys (who did much more close work).

8. However, the same was seen to be true of the non-Jewish boys (who did not do an excessive amount of close work) as compared with the non-Jewish girls.

9. It was suggested, therefore, that there was a sex-determined factor which controlled the growth of the eye.

10. The excessive incidence of myopia among Jewish boys was explained by the racial factor, and the greater prevalence of low hyperopia by the sex-determined (and non-racial) factor, which allowed for a greater development of the length of the eye.

According to Posey, the shape of the skull frequently determines the conformation of the orbit, which, in its turn, molds the form of the eyeball. Myopia, therefore, occurs most commonly in races like the Teutonic, whose skulls are long in the anteroposterior diameter, and is but rarely met with in the Negro and the Indian. in whom the converse is the rule.

Vandergrift also expressed the belief that myopia is usually associated with brachycephalism, while hyperopia occurs with dolichocephalism. He also said that myopia may begin in infancy with a change of the shape in the eyeball through pressure of the external muscles to supplement insufficient action of the ciliary muscle.

ACQUIRED CONDITIONS

Kassas denied any hereditary influence whatever on the development of myopia. He expressed the opinion that this form of refraction depends solely on unhygienic conditions of the environment, especially in the school. He ascribed to syphilis and tuberculosis in the parents a predisposing factor, and a similar rôle to measles.

Nicolato held that there must be some common cause as a predisposing factor in all myopias, and that this factor is an endocrine disturbance, which affects the nutrition of the eye. The endocrine alterations are hereditary and are sometimes complicated by various diatheses. The resulting myopia may be benign or pernicious, and the predisposing cause of all myopia is a thymic dysfunction.

Leoz Ortin expressed the belief that the choroidal lesions in myopia are due to arteritis of a more or less sclerosing nature and, probably, to a special predisposition of the choroidal vessels since youth. As the changes are almost always found in the posterior part of the eye, it is probable that the sclerosis attacks especially the short posterior ciliary arteries, each one of which has a special territory and, although not entirely independent, communicates with the others by capillaries and not by larger anastomotic branches. Leoz Ortin considered alcoholism, syphilis, rheumatism, gout, diabetes, tuberculosis, chemical intoxications, acute intoxications and, especially, heredity as the predisposing factors which are intensified by diminished vitality. He also held that the thinness of the sclera in myopia is probably due to a process of scleromalacia.

Sonder expressed the opinion that the diseases of childhood are the cause of myopia. Of a hundred cases of progressive myopia, one or more of such diseases have occurred in every case. Sonder's conclusion is far from satisfying, as there are few children who have been free from the diseases of childhood, and yet not all children have myopia.

Wernicke maintained that malignant myopia and glaucoma are both manifestations of one and the same process.

Argañaraz regarded myopia, especially that which is accompanied by pronounced bulging of the posterior pole of the eye, as having the same origin as the ectasia of the anterior pole which constitutes keratoconus. He held that both conditions are due to a disturbance of the

internal secretions, and he stated that in the great majority of cases of keratoconus and high myopia, clinical examination reveals the existence of heredosyphilis.

Lemere reported a number of cases, suggesting that infections of the nasal sinuses may be an important factor in weakening the sclera and in producing myopia.

Myopia, according to Keith, is a disorder of growth. After the twentieth year, elongation of the eyeball may continue in those who become the subject of myopia in childhood or in adolescence, but Keith can find no data to lead him to believe that an eye which remained normal until the twentieth year can thereafter undergo the changes which produce myopia. He therefore concluded that the causes which produce myopia are operative in the growing eye, and that myopia should be ranked among the disorders of growth. Keith suggested that just as in acromegaly the activity of the fibroblasts is entirely thrown out of gear by some defect in the secretion of the pituitary body, so some comparable fault in the mechanism which normally regulates the growth of the sclera must be the root of myopia.

Wiener has recently published his results of the use of epinephrine in progressive myopia. He expressed the belief that there is a certain type of progressive myopia which is favorably influenced by exercise and local instillations of epinephrine.

Heinonen was not satisfied that close work is the most important factor in myopia. He expressed the belief that the intellectual endowment of the person is intimately bound up with myopia.

Straub held that the psychic factor determines the type of refraction a person will have. The state of refraction is not attained mechanically by the mere trend of hereditary development, but intelligently. Only those who desire to see clearly at a distance are able to make their eyes emmetropic or to maintain them so, if that form of refraction has been attained by chance. But where this psychic element is wanting, the adjustment fails and hypermetropia develops, or myopia when the attention is attracted too constantly to near objects. Straub is against all theories of an exclusive hereditary nature.

Druault-Toufesco considered that there is a marked difference between the psychism of a myope and that of a hyperope; they neither reason, work, write nor draw in the same way. Two persons of like refraction understand each other better than those whose refraction differs. Various differences between the mental make-up of the myope and the hyperope are traced. The author claimed that it is possible to recognize from the style of writing whether the writer is myopic or hyperopic, and the works of art bear the clear imprint of the artist's refraction.

Brückner and Franceschetti described twenty-five cases of high myopia in childhood which they consider to be a distinct type from the myopia that increases during school age. They termed this condition "infantile myopia." Two thirds of the patients were boys, and the rest were girls. All of the children were from 6 to 8 years of age. They showed myopia that ranged from 3 to 25 diopters and a myopic astigmatism from 1 to 4 diopters. All of these children had a characteristic ophthalmoscopic picture: The disk was oval and bordered on the temporal side by a small conus, which seldom exceeded more than a third of the diameter of the disk. Occasionally, beyond this, there was an area of peripapillary atrophy of the pigment epithelium. The pigment epithelium was largely absent between the disk and the macula, and, in fact, through the whole posterior pole of the eye. The pigment in the macular region, however, was increased, so that a dark pigmented spot was characteristically found. The retinal reflexes were characteristic by their absence, and the blood vessels showed small light streaks.

The visual acuity of these children was never normal even with the best correction, and the higher the myopia the poorer was the vision. The visual fields and the dark adaptation were within normal limits.

A distinct hereditary influence could be traced only in a few of the cases. For the most part, the parents were not near-sighted, nor were other children in the same family. The authors could say little of the rate at which the process developed. One patient who had been observed for eighteen years showed practically no change in refraction from a myopia of 9 diopters. On the other hand, one patient showed an increase of 11 diopters over a period of twenty-one years. The authors felt that the use of the eyes had nothing to do with the increase of the myopia. Practically all exogenous factors could be ruled out.

Brückner and Franceschetti considered the myopia as strictly axial, since no change in the curvature of the corneal surface and no evidence of change in the curvature of the lens or of indicial myopia could be found. They regarded the characteristic pigmentary changes in the back of the eye as having something to do with the development of the myopia, but in just what way, they were not sure. They were of the opinion that the pigment changes were not the result, however, of stretching of the ocular coats.

Li ascribed the high percentage of myopia in Chinese students (53 per cent) to the peculiar construction of the Chinese characters, writing them being more difficult than reading them. Poor hygiene generally prevailed among the students.

My own experience makes me doubt whether the Chinese characters are fully responsible for the high percentage of myopia seen in the

Chinese race. A few illustrations from my records of myopia in Chinese children will suffice:

Child aged 5 years: O. D. —6.00 D. S. ⌒ —4.00 D. cyl., ax. 180.
O. S. —6.00 D. S. ⌒ —4.00 D. cyl., ax. 180.

Child aged 6 years: O. D. —10.00 D. S.
O. S. —10.00 D. S.

Child aged 6 years: O. D. —14.00 D. S. ⌒ —2.00 D. cyl., ax. 180.
O. S. —20.00 D. S. ⌒ —2.00 D. cyl., ax. 180.

Child aged 10 years: O. D. —7.00 D. S. ⌒ —2.00 D. cyl., ax. 180
O. S. —7.00 D. S. ⌒ —2.00 D. cyl., ax. 180.

Child aged 10 years: O. D. —7.00 D. S. ⌒ —1.50 D. cyl., ax. 80.
O. S. —7.00 D. S. ⌒ —1.50 D. cyl., ax. 135.

Child aged 7 years: O. D. —10.00 D. S. ⌒ —2.00 D. cyl., ax. 15.
O. S. —11.00 D. S. ⌒ —1.50 D. cyl., ax. 165.

Child aged 10 years: O. D. —11.00 D. S. ⌒ —1.75 D. cyl., ax. 15.
O. S. —11.00 D. S. ⌒ —3.00 D. cyl., ax. 165.

The last two children were sisters.

THE NORMAL EYE

The question of what is a normal eye is still not well settled. The hyperopic eye has been spoken of as the short eye from before backward and the myopic eye as being too long. Tron recently showed that the hyperopic eye measures between 19 and 24 mm., about as held heretofore, but that the emmetropic eye might also be as short as 20.46 mm. or as long as 25.46 mm. and, what was more at variance with the previous views, the myopic eye might be less than 22 mm. in length. In this short eye the myopia was determined by a sharp curve of the surface of the cornea or lens, or both.

Steiger said that emmetropia cannot be regarded as the normal refraction with any more reason than, for example, that 5 feet, 6 inches could be regarded as the normal height of the human species. Newborn infants offer the best statistical material; even among these are large congenital differences. The refraction of the eye does not show whether it is pathologically elongated; a hyperopic eye may be elongated, and a myopic eye may be of normal length.

COMMENT

In reviewing the various theories proposed to explain myopia, one is impressed by the fact that none of them satisfactorily offers an explanation for this condition. The mechanical theories are far from satisfactory. A great deal can be said for the theory of heredity, but accepting myopia as hereditary is merely begging the question. A great deal can be said for the acquired basis of myopia. Probably myopia is not caused by any one single factor, but by a number of various factors.

In reviewing the various theories, one is further impressed by the fact that the majority of the writers make no attempt to differentiate between true or low myopia, that is, from 1 to 6 diopters, and high myopia, so-called progressive myopia, school myopia and work myopia. Most of the writers confuse the two conditions.

The reason is obvious, as no definite division can be made between the two conditions. Parsons stated that it is impossible clinically or pathologically to draw a distinct line of demarcation between the two forms. Jackson was more emphatic, when he said: "All cases of myopia are 'progressive' at the start and cease to be so when the conditions that produce myopia are removed." He further condemned the use of the terms "malignant," "pernicious" and "progressive." The value of the proper treatment of myopia has been well outlined by Jackson.

Nevertheless, there is a definite myopia which reaches a low degree and remains stationary, whether the person wears glasses or not, and whether he uses his eyes for close work or not. I can best illustrate it by my own case. I am myopic and did not secure glasses until I graduated in medicine, twelve years ago. I always knew that I could not see well and distinctly in the distance. I never did see the writing on the blackboard, and was aware when attending the theater or an outdoor event that I did not make out distinctly the persons participating. At no time did I have any discomfort with my eyes. My original correction for each eye was —1.50 D. S. ⌒ —0.50 D. cyl., ax. 90. I have been refracted since then a number of times, and there has been practically no change in my error of refraction. There is no doubt that my form of myopia may be considered as true or low myopia.

Of course, I fully realize now that there would have been many advantages if I had secured glasses early in life and had seen things in the distance as an emmetropic person does.

According to Fuchs, the lower degrees of myopia may be considered physiologic, being the result of a regularly occurring but overacting developmental process, and in its high degree it is associated with changes in the background of the eye and must be regarded as pathologic.

Before any progress can be made at arriving at the etiology of myopia, it is absolutely necessary to differentiate between low and high myopia; the two are probably separate entities.

LOW MYOPIA

Low myopia, as Fuchs has stated, may be regarded as physiologic. It is possible that low myopia is an evolutionary change in the darwinian sense, and it is nature's adaptation of the human eye to a continually increasing degree of culture. Although low myopia may be

considered a harmless adaptation, I do not consider it an ideal one. Emmetropia is the ideal condition of an eye.

However, nature does not always work toward the ideal. Insects, fishes and frogs are myopic. A fish's eye is myopic when in water; far-sight would be useless to it, since it is unable to see far in the water. A frog does not need to stare at the moon; his business is to catch flies when they come into his close range. When it comes to birds and large mammals, the condition is reversed. The first is sharp-sighted, and the latter to a lesser degree. Savages are practically free from myopia. New-born infants rarely show myopia ophthalmoscopically. On the other hand, older children and adults of cultured races have a considerable degree of myopia. To the savage excellent far-sight is essential to obtain his food, and keen vision is necessary to protect him from his enemies. To the modern man distant vision is not as essential as it was to the savage man. Modern life demands good vision for close work, as most of the work done at present is performed at close range. Myopia is frequently found among cultured classes and more commonly in those engaged in intellectual pursuits. (By cultured classes is meant here not only the highly educated, but all who continually apply themselves to fine and minute work.) Birnbaum suggested that the survival of the fittest may have helped to eliminate the myopes in savage races and to preserve them in the civilized races. Keith, speaking of our forefathers, said: "We cannot believe that a myopic ancient could have survived. We therefore presume that in prehistoric times cases of pronounced myopia must have been unknown or very rare."

Two diopters of myopia gives comfortable eyes for close work and practically does away with the necessity for glasses for close work during the presbyopic stage. That low myopia is often higher than 2 diopters is one of the unfortunate things in the evolutionary process. It is well known that very young children are hyperopic, and during their growth a great many of the hyperopes have a tendency to lose their hyperopia and become myopic or emmetropic. Children who become myopic have a low hyperopia early in life, and if they lose this hyperopia they become myopic. For example, if the child had 3 diopters of hyperopia and loses this amount he will become emmetropic. On the other hand, if the child has 1 diopter of hyperopia and loses 3 diopters, he will have a myopia of 2 diopters. The work of Sourasky illustrates well this condition among Jewish children, in whom myopia is common. These children have a low hyperopia early in life and become myopic later in life. Myopia has probably nothing to do with close work. It is part of the inherited make-up of the person. Children do not become myopes because they use their eyes a great deal for study and reading. It is possible that they study and read a great deal

because they are myopic. Myopes take up intellectual pursuits because myopia is probably part of their intellectual endowment.

HIGH MYOPIA

High myopia offers a different problem, and one should consider it, as suggested by Fuchs, as pathologic. The cause of high myopia is still obscure. In such cases the use of the eyes for close work probably has an influence on the progress of the condition, although some of the worst cases of myopia occasionally seen are among the illiterates. I have already mentioned the Chinese children between the ages of 5 and 10 who have myopia ranging from 7 to 20 diopters. It is difficult to conceive just how the use of the eyes in such young children, especially those of 5 and 6 years, could be responsible for such a high degree of myopia. Whether it is due to a glandular disturbance, poor hygienic conditions, faulty metabolism, a lack of the necessary vitamins, disease of the eye itself or other conditions still has to be worked out. Sir Arthur Keith stated that myopia is a disorder of growth, and suggested that the essential cause of myopia must be sought in the behavior of the fibroblasts which are not only the bricklayers but also the architects who erect the edifice enclosing the structure of the eye. "If the sclerotic fibroblasts lay sound material and lay it rightly, then all is well, whatever may be the usage we give our eyes. But if the material is unsound and laid wrongly, then it is possible that forces which leave the normal eye unaffected may damage the abnormal eye."

GENERAL COMMENT

The explanation of high myopia still remains to be given. In high myopia one deals with a diseased eye. Donders, as early as 1864, said: "I have no hesitation in saying, that a near-sighted eye is not a normal eye. In it there exists more than a simple anomaly of refraction." As Turner has stated: "To merely prescribe lenses is an evasion by which the patient is frequently given a sense of security not warranted by facts." I think that high myopia not only is an ophthalmologic problem, but is a medical problem in which the pediatrician, internist and biochemist are needed to solve the problem.

From a practical point of view differentiation between true and high myopia is of the greatest importance. Parents are often greatly worried by the fact that their child is near-sighted, and usually the near-sighted child is fond of reading. They often blame the close work as the cause of the child's myopia. Often the problem comes up as to whether a myopic child should take up a certain vocation. If the child has true myopia, one can assure the parents that the myopia is part of the child's make-up and no restriction should be placed in the child's way regarding

his close work and study. Proper glasses with full correction should be prescribed and worn at all times, as many observers believe that the glasses have a tendency to diminish the progress of myopia.

In cases of high myopia, children should be sent to special sight-saving classes in public schools (Rodin), in which the use of the eyes is restricted and in which special large type textbooks, large pencils, special paper, etc., are used. Vocations demanding a great deal of use of the eyes should be discouraged. Children with high myopia should be placed in the hands of pediatricians for such attention as may be indicated.

SUMMARY

1. The modern theories of the etiology of myopia are reviewed.

2. The causes of myopia can be roughly divided into mechanical, hereditary and acquired.

3. None of the theories proposed offers a satisfactory explanation of myopia.

4. Most writers confuse between true or low myopia and high myopia.

5. Low myopia is from 1 to 6 diopters.

6. Low myopia is probably an evolutionary change and is nature's adaptation of the human eye to a continually increasing degree of culture.

7. High myopia represents a diseased eye.

8. The difference between low and high myopia is important, as the two are probably separate entities.

9. High myopia should be considered as a disease of the eye.

10. The etiology of high myopia still remains to be solved. The aid of the pediatrician, internist and biochemist is necessary to help in the solution of this problem.

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News and Notes

EDITED BY DR. JOHN HERBERT WAITE

SOCIETY NEWS

Ophthalmological Society of the United Kingdom.—The annual congress of the society will be held in London on May 11, 12 and 13, 1933. Prof. Reginald Punnett, F.R.S., will read a paper on "Mendelism," which will be followed by a discussion on the subject "Heredity and Eye Diseases," to be opened by C. H. Usher, M. van Duyse and Ida C. Mann. The annual dinner of the society will be held on Thursday, May 11.

GENERAL NEWS

Annual Spring Graduate Course.—The seventh annual spring graduate course of the Gill Memorial Eye, Ear and Throat Hospital will be held April 3 to 8, 1933, at Roanoke, Va. The guest members in ophthalmology are: Dr. Webb W. Weeks, New York; Dr. Ralph I. Lloyd, Brooklyn; Dr. David W. Wells, Boston; Dr. H. S. Hedges, Charlottesville, Va., and Dr. John A. Pilcher, Jr., Roanoke, Va.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

THE TOPOGRAPHY AND ANATOMY OF THE ORA SERRATA AND THE ORBICULUS CILIARIS. RICHARD STEIN, Arch. f. Augenh. **106:** 145, 1932.

The author measured the distance of the ora serrata from the limbus in sixty eyes the axial length and refraction of which varied. He found that the distance of the ora serrata from the limbus varies directly with the axial length and within certain limitations with the refraction of the eye. The accompanying table illustrates this point.

Axial Length of Eye, Mm.	Refraction	Average Distance of Ora Serrata from Limbus, Mm.	
		Temporal	Nasal
21 to 23	Hyperopia, 7 to 2 diopters	5.5	4.8
23 to 24.5	Hyperopia, 2 diopters to emmetropia to myopia 2 diopters	7.0	6.3
24.5 to 26.5	Myopia, 2 to 10 diopters	8.1	7.0
27 to 34	Myopia of 10 diopters	9.5	8.8

The distance of the ora serrata from the limbus is slightly greater on the temporal side than on the nasal side.

F. H. ADLER.

DEVELOPMENT OF THE CORNEA, SCLERA, CONJUNCTIVA, AND PUPILLARY MEMBRANE. R. SONDERMANN, Arch. f. Ophth. **128:** 119, 1932.

The author's conclusions are: The substantia propria of the cornea is formed by scleral fibrillae of connective tissue, which at the beginning of the second month commence to grow forward and thus cut into the mass of epithelial cells formed by the ectoderm and the lens vesicle before its separation from the surface. Posteriorly to this layer of connective tissue the epithelium degenerates, thus favoring the complete separation of the lens vesicle from the ectoderm. Only a thin layer of epithelial cells remains on the posterior surface of the anlage of the corneal substance, which later is transformed into endothelium. The embryology of the tissues participating in the formation of the limbus is thoroughly discussed. The author recommends dropping the term "anterior vitreous," because he thinks the substance is mainly an artefact which only superficially resembles the real vitreous.

P. C. KRONFELD.

Conjunctiva

A Peculiar Form of Pigmentation of the Conjunctiva in the Disease Produced by Vitamin A Deficiency in Adults. A. Pillat, Arch. f. Ophth. **127:** 575, 1931.

This paper represents the first detailed description of this disease, which is quite frequently found in China. A typical case is first cited: A Chinese student, aged 23 years, was confined to a penitentiary for one year. At first his food consisted of rice, white bread and white Chinese cabbage, which contains very little vitamin. Later he received only very little rye bread and some vegetables preserved in salt water. The water supply also was deficient. At the end of the first half year of imprisonment, hemeralopia developed; later the vision also became poorer in daylight. The clinical diagnosis was xerosis of the conjunctiva bulbi and of the cornea; the conjunctiva was heavily pigmented. The pigment was gray and most marked around the inner canthus (the semilunar fold, caruncle, lower fornix and nasal portion of the tarsal conjunctiva of the lower lid). The cornea remained free from pigment. The pigmentation of the conjunctiva consisted of fine "flour-like" dots in the epithelial cells and of larger conglomerations in the subepithelial tissue.

Children never show this pigmentation because they usually die from the deficiency disease before the pigmentation has had time to develop. In adults the pigmentation occurs in a relatively early stage of the disease and parallels its course. It always disappears if the underlying deficiency is remedied. It occurs among the "pigmented" races (Chinese), and also among Europeans.

P. C. Kronfeld.

A Case of Ocular Myiasis. A Kreiker, Arch. f. Ophth. **127:** 644 (Dec.) 1931.

A man who was lying outdoors on a couch for treatment of pulmonary tuberculosis had a sensation as though a flying insect struck his eye. A few minutes later he felt sharp pain, looked at his eye and found numerous rapidly moving "worms" in the lower fornix. The author diagnosed them as fly larvae, and found it impossible to remove them with a forceps because they hid in the fornix when he directed the light at them, and clung to the conjunctiva with their maxillary hooks.

He instilled paraffin oil every hour for the rest of the day. This entered the trachea of the larvae and choked them, after which they were easily removed. There were over thirty larvae. It could not be determined to which variety of flies the offending insect belonged. It must have been a variety in which the eggs are hatched while they are still in the vagina.

P. C. Kronfeld.

Nodule-Like Conjunctivitis Produced by Fat Impregnation. R. Schneider, Ztschr. f. Augenh. **75:** 369 (Nov.) 1931.

A conjunctivitis that has the appearance of the papillary hypertrophy of trachoma is described. The superficial layers of the conjunctiva of the tarsus are covered with small yellowish-gray protruding bodies that

are surrounded by a network of blood vessels. The retrotarsal fold is hyperemic and swollen and the conjunctiva of the lower lid free from papules. Elschnig described the first case of this type of inflammation of the conjunctiva. Schneider believes that the lesion is produced by the use of poor fat menstrums for ocular medication. The combination acts as a foreign body and produces a traumatic conjunctivitis.

A. M. YUDKIN.

Cornea and Sclera

A CASE OF TRAUMATIC "IMBIBITION" OF THE CORNEA. A. LOEWENSTEIN, Arch. f. Ophth. **127:** 598, 1931.

A few hours after injury with a blunt object, a woman, 30 years of age, showed a disk-shaped opacity (3 mm. in diameter) in the center of the cornea which protruded slightly above the level of the cornea and was surrounded by a yellow reflex. Forty-eight hours later the cornea was again normal. The opacity apparently was produced by aqueous entering the stroma without breaks in Descemet's membrane; the yellow reflex was produced by a mirror action of the corneal lamellae at the bending point. The corneal endothelium is of great importance for the metabolism of the whole eye because of its selective permeability. It is highly improbable that the corneal opacity that occurs after a blunt trauma without tears in Descemet's membrane is produced by simple imbibition because the composition of the aqueous and that of the fluid in the cornea are about the same. It is more likely that a precipitation process takes place in the cornea as the result of the impaired filter action of the endothelium.

If the same process takes place in the lens, the changes are irreversible. The author explains this as the result of a difference in the regenerative power between lens epithelium and corneal endothelium.

P. C. KRONFELD.

OPERATIVE THERAPY OF KERATOCONUS: REPORT OF A CASE. A. VOGT, Klin. Monatsbl. f. Augenh. **87:** 258 (Aug.) 1931.

A woman, aged 30, had keratoconus which progressed to from 60 to 70 diopters with 6 diopters astigmatism in her left eye within ten years, also beginning keratoconus in her right eye for two years and a half. The apex of the conus of the left eye, the vision of which could not be improved with glasses, was cauterized with the result that the refraction decreased to 34 diopters within three weeks. It increased again to 44 diopters within the following weeks, while the astigmatism nearly disappeared. The final result was a small central scar and vision of 0.5 with 1 diopter concave spheric combined with 1 diopter concave cylinder. Vogt emphasizes the importance of a well defined perforation coupled with permanent full mydriasis by atropine and an epinephrine substitute prior to the operation, likewise for a few weeks afterward, so as to avoid anterior synechiae.

K. L. STOLL.

SEVERE TROPHIC CORNEAL DAMAGE IN A CASE OF ARSPHENAMINE DERMATITIS. H. SAUFERLIN, München. med. Wchnschr. **79:** 1476 (Sept. 9) 1932.

A case report of this unusual complication is preceded by a survey of the literature of like conditions, and a comprehensive bibliography is appended. The outstanding features of the author's case were the severe damage to the cornea without previous visible inflammation of the eye and the surprising rapid involvement in spite of careful ophthalmologic supervision. Because of the absence of reaction, together with the finding of an ulcer involving the entire thickness of the cornea, a diagnosis of trophic corneal abscess was made by the ocular department. The patient, aged 43, received one injection of 0.3 Gm. and seven of 0.45 Gm. of neoarsphenamine, together with fifteen injections of bismuth, in a period of six months. The day following the last injection of arsphenamine a rash appeared on both arms which spread in two days to the neck, breast and face. Local treatment did not help. The tongue was swollen, and the mucous membrane of the mouth was reddened. The temperature was 39 C. (102.2 F.) and the pulse rate, 100, which increased to 39.5 C. (103.1 F.) and 110, respectively on subsequent days. There was a mild conjunctivitis not involving the cornea, which responded to treatment quickly with some recurrence. Six weeks later the patient suddenly complained of a severe pain in the right eye. Examination revealed a perforation of the cornea parallel to the limbus from 11 to 12 o'clock with a prolapsed iris. A fine powder-like clouding of the entire cornea was noted. The iris prolapse was excised and a conjunctival flap thrown over the perforated area. The dermatitis subsided under treatment with injections of sodium thiosulphate. A visual acuity of 5/60 was obtained in the affected eye. The author believes that the reaction was due to accumulative effects of the arsphenamine. The conjunctivitis is construed as the first sign of an overdose.

L. L. MAYER.

Experimental Pathology

HISTOLOGIC AND CLINICAL PHENOMENA CONNECTED WITH ACUTE LOCAL DERANGEMENTS OF THE CAPILLARY CIRCULATION IN THE EYE. F. POOS, Arch. f. Ophth. **127:** 489, 1931.

Any stimulus producing inflammation leads to atony (complete relaxation) of the capillaries, consisting of maximal dilatation and increased permeability. The blood within those capillaries is concentrated and the circulatory resistance increased. Proteins enter the tissues, thus diminishing the colloid-osmotic gradient between the blood and tissue. The author studied these changes on animal eyes after the application of various physical, chemical and nervous stimuli. Puncture of the anterior chamber also produced an acute severe disturbance of the circulation in the capillaries, which lasted for several days. A normal human eye that had to be enucleated because of an orbital sarcoma was subjected to two punctures of the anterior chamber and then removed. On histologic examination it showed the same changes as those found in animal eyes, though less intensive. The regenerated aqueous of animals proved to be very toxic, and produced definite

inflammation if injected subconjunctivally into animals of the same species. This toxicity apparently was caused by cleavage products of the protein molecule. Most of the alkaloids also produced capillary disturbance, with all its consequences, if they were introduced into the eye in sufficient concentrations (subconjunctival injection). In all those experiments a typical intra-ocular tension curve accompanied the phenomena of capillary upset, which was thoroughly studied by the author. He concludes that variations in the size of the pupil, the caliber of the intra-ocular vessels, the tone of the vessel wall, the behavior of the ciliary epithelium and the condition of the tunica sclerotica are of minor importance for the mechanism of the reactive fluctuations of the intra-ocular tension. The main factor, in his opinion, is the disturbance of capillary circulation.

P. C. KRONFELD.

HYPOTONIA FOLLOWING HYPERTONIA. K. VOM HOFE and H. HARTUNG, Klin. Monatsbl. f. Augenh. **87**: 486 (Oct.) 1931.

Several ophthalmologists have doubted the results of former experiments of the authors. These experiments showed that a longer or shorter period of hypotonia followed transient hypertonia after injections of physiologic solution of sodium chloride into the vitreous of rabbits. Consequently a new series of experiments was performed by the authors, with the following result: Five-hundredths cubic centimeter of physiologic solution of sodium chloride injected into the vitreous of rabbits produced increase of the intra-ocular tension, which lasted a short time and was followed by hypotonia of varying duration; the hypotonia was in evidence even when the tonometer was used only once a day. If the needle was introduced into the vitreous and removed at once, without injecting any fluid, the intra-ocular tension remained unchanged. Luxation of the eyes, lasting ten minutes, will produce first an immense increase of the tension, resembling that observed after injections into the vitreous; this increase is followed by hypotonia, amounting to about one half of the original tension, and lasting about four days. Histologic examination of eyes enucleated five or more days after the injection showed inflammatory changes in the anterior and posterior segments of the globe, in accordance with the observations of Poos.

This recent series of experiments demonstrated again the fact that hypertonia, suddenly produced, is followed by hypotonia, lasting for a longer period. The eyes receiving the injection became softer, although their contents were augmented by the quantity of fluid injected. Vom Hofe explained the hypertonia as an overextension of the globe, coupled with reactive dilatation of the vessels, resulting through the increased contents of the globe.

K. L. STOLL.

General Diseases

OXYCEPHALY AS A PATHOGENIC ENTITY. A. N. BRONFENBRENNER, Am. J. Dis. Child. **42**: 837 (Oct.) 1931.

In the study of a series of clinical cases of oxycephaly as well as the data reported in the literature, Bronfenbrenner noted certain characteristics of a compensatory adjustment mechanism: When a premature closure of the coronary skull suture occurs, it impairs the normal adaptability of the skull to the growing brain of a child, and an effort to meet

the demands of the growing brain brings about the oxycephalic deformity. Factors of the premature synosteosis and the subsequent compensatory struggle may naturally damage the brain and its adjacent parts. Most frequently the optic nerve undergoes severe atrophic changes. The degree of the damage sustained by the entire brain bears a direct relation to the efficiency of the compensatory process: the less effective has been the compensatory mechanism and, thus, the less outspoken are the morphologic features of oxycephaly, the greater the brain drainage to be expected. Hence, a marked mental defect is found in rather mild, atypical instances of oxycephaly (and allied deformities of the skull), while in cases with outspoken oxycephalic features a mental defect might not enter into the clinical picture at all. Various intracranial infectious processes appear to be the main etiologic factors in the premature skull synosteosis of oxycephaly and allied deformities of the skull. The cases reported by the author emphasize the importance of tuberculosis and especially syphilis as probable etiologic factors of oxycephalic deformity.

[J. A. M. A.]

OCULAR DIABETES. H. ARRUGA, Arch. de oftal. hispano-am. **33**: 356 (July) 1932.

The frequency of the ocular complications in diabetes as found by the author in twenty thousand patients coincides with Uhthoff's statistics.

The cases of cataract are mostly of senile variety associated with diabetes. Pure diabetic cataract is rare. It is at first subcapsular. The operative indications in each case must be solved by the oculist and the internist, the former being guided by the condition of the retina and the ocular tension, the latter by the general condition of the patient. It is necessary to normalize the arterial tension; to avoid acetonemia or acidosis and to reduce glycemia to its normal limits, placing the patient in the best possible conditions for defense. When a high arterial tension persists, notwithstanding proper diet and treatment, bloodletting half an hour before the operation is indicated.

Diabetic retinitis is most serious when associated with hemorrhagic glaucoma. It is the consequence of sclerosis and degeneration of the retinal blood vessels. The amount of blood sugar bears no relation to its production. It is often associated with albuminuria, and it is often difficult to determine which is the responsible etiologic factor. From a pathologic point of view the lesions consist of an obliterating arteritis with fatty degeneration, sclerosis of the vessel walls and hemorrhages.

In retinal lipemia, which is very rare, hemorrhagic glaucoma is a most serious complication, bringing about loss of sight and often of the eye. It is the result of advanced sclerotic vascular lesions with a hemorrhagic tendency.

The author next discusses iritis, retrobulbar neuritis, refractive disturbances, ocular paralyses and hypotonia in connection with diabetes. Hypotonia is found in all cases of diabetes (Heine) and is of great diagnostic value.

In connection with the prognosis, the author points out that two thirds of the patients die within two years. C. E. FINLAY.

Glaucoma

THE FILTRATION OPERATION OF MAUKSCH FOR CHRONIC GLAUCOMA WITH PRELIMINARY REPORT ON TWENTY-FOUR OPERATIONS. G. F. SUKER, Am. J. Ophth. **14:** 732 (Aug.) 1931.

The author briefly discusses the various operations for glaucoma and reviews the technic of the Mauksch operation. A table is given showing the results as to vision, tension, etc. The average reduction in tension was from 25 to 30 points (Gradle, Schiötz). Twenty-four eyes were operated on, the results in twenty being considered successful.

W. S. REESE.

THE CENTRAL AND PERIPHERAL LIGHT SENSE IN CHRONIC SIMPLE GLAUCOMA. G. ZANETTIN, Ann. di ottal. e clin. ocul. **59:** 847 (Sept.-Oct.) 1931.

Previous work on the light sense in glaucoma is reviewed. In nearly all investigations only the light sense in central vision was investigated. The author made use of a special adaptometer with a tube and diaphragm admitting a measured amount of light. This was moved on the arms of a special perimeter, so that the light sense was estimated not only for the fixation point but in the horizontal meridian at 30 and 50 degrees and in the vertical meridians at 20 and 40 degrees from the center. These points were chosen as corresponding to the various zones of peripheral visual acuity as determined by La Cascio. Determinations were made after one-half hour in the dark room, first on ten normal persons and then on seventeen eyes of thirteen glaucomatous patients.

The resulting curves varied greatly, not only between two eyes of the same person, but also in the same eye on different occasions. No relation of light sense to the visual acuity preserved was noted, some patients with poor central vision having fairly good central light sense.

There was a definite relation, however, of both visual fields and tension to the light sense. This was reduced in areas of the field where no perception of colors was present, although there were some variations in the light sense in some apparently intact parts of the field. The relation to tension observed was that eyes with high tension usually showed marked reduction in light sense, and that in apparent exceptions to this the time during which the tension had been elevated was not long. In some cases a definite improvement in light sense was seen to follow successful operations to reduce tension. In two cases of definite glaucoma a normal central light sense was found, but in all cases there was more or less reduction in peripheral light sense and in most early cases a reduction also in central light sense. The reduction was most marked in the temporal parts of the field, then in the superior, inferior and nasal parts in order. The author concludes that changes in the light sense occur in the earliest stages of glaucoma, but that no prognostic value could be attached to them.

S. R. GIFFORD.

A Clinical Study of the Influence of Subconjunctival Injection of Ergotamine Tartrate (Gynergen Brand) on the Intra-Ocular Tension in Glaucoma. Sigurd Werner, Acta ophth. **9:** 286, 1931.

In view of the disappointing results obtained with subcutaneous injections of ergotamine tartrate (gynergen brand), Werner used a subconjunctival injection of the drug in a group of eighteen cases of glaucoma to see whether it would produce more favorable reduction of intra-ocular tension. In fourteen eyes the tension was reduced but the effect lasted for one or two days. The best results were obtained in glaucoma simplex. The reduction of intra-ocular tension by subconjunctival injection was not as favorable as that produced by miotics or epinephrine, but it was better than the subcutaneous method.

A. M. Yudkin.

Ocular Muscles

Paralysis of Ocular Muscles Following Spinal Anesthesia. J. Biggam, Brit. J. Ophth. **16:** 552 (Sept.) 1932.

Five cases of paralysis of one or another of the rectus muscles of the eye following the use of stovaine as a spinal anesthetic are reported. Although this agent has been extensively used at the hospital since 1915, no other instance of paralysis of ocular muscles was recorded, with the exception of the five cases that occurred early in 1927.

The occurrence of this isolated group suggests the presence of some toxic element in the drug in use during this period. The patients complained of headache, usually severe, which preceded the onset of the paralysis by one or seven days. The headache lasted from one to three weeks. The paralyses were maximal at their onset, remained stationary for varying periods and then gradually improved.

In one case the paralysis occurred not more than two days after the administration of the drug. In no case was any other abnormality discovered.

W. Zentmayer.

Orbit, Eyeball and Accessory Sinuses

Pulsating Exophthalmos. G. L. King, Am. J. Ophth. **14:** 786 (Aug.) 1931.

Two cases are reported. This article is mainly statistical from the standpoint of treatment, 679 cases being considered, data of which were obtained through reported cases and by questionnaire. The following summary is given. 1. A general résumé of the subject of pulsating exophthalmos is given, with a review of the literature up to the present time, comprising a total of 616 reported cases. 2. Two new cases are recorded. One patient was treated by ligation of the internal carotid followed by hemiplegia and death; the other was untreated and recovered, at least temporarily. 3. Results of a questionnaire on the subject are tabulated.

W. S. Reese.

The Pupil

MAINTENANCE OF IRIS SPHINCTER TONE IN THE RAT. M. F. HEIDGEN and R. D. BARNARD, Am. J. Physiol. **98:** 276, 1931.

The authors instilled a variety of anesthetics into the conjunctival sac of adult white albino rats, tested corneal and conjunctival anesthesia and noted the degree of mydriasis produced. In several animals the ophthalmic branch of the fifth nerve was cut and in others the gasserian ganglion ablated. In five animals 2 per cent butyn was injected into the gasserian ganglion. The results indicated that the pupilloconstrictor tone in the rat is maintained partially, at least, as a reflex involving afferent fibers of the fifth nerve.

The anesthesia produced in a variety of ways always caused a mydriasis, although it did not interfere with the light reflex. The mydriasis produced was not maximal unless the animal was placed in the dark. The pupillary tone, therefore, in the rat is apparently a summation of impulses generated in the retina by light and in the sensory structures in and around the eyeball. The iris control in the rat differs, therefore, from that in the dog, rabbit and man in having a mechanism the tone of which is controlled in part by sensory impulses arising in the eye and orbital tissues.

F. H. ADLER.

PUPILLARY DILATATION PRODUCED BY DIRECT STIMULATION OF THE TEGMENTUM OF THE BRAIN STEM. W. R. INGRAM, S. W. RANSOM and F. I. HANNETT, Am. J. Physiol. **98:** 687, 1931.

Karplus and Kreidl located a center for the reflex dilatation of the pupil in hypothalamus. They found that direct faradic stimulation of the medial and rostral part of the subthalamic nucleus produced the same effect on the eye as the stimulus applied to the cervical sympathetic trunk. Other authors have confirmed their work, but the present investigators find that dilatation of the pupils can be obtained from a good many other regions in the brain beside the subthalamic nucleus. They stimulated various parts of the brain stem and ventral parts of the diencephalon with a faradic current of low intensity, using the Horsley-Clarke stereotaxic instrument and bipolar needle electrodes (*Brain* **31:** 45, 1908).

Dilatation of the pupils could be obtained from all points in the tegmentum of the mesencephalon and pons. The instrument used prevented the spread of the current.

F. H. ADLER.

VOLUNTARY MYDRIASIS. A. PETROVIČ AND A. TSCHEMOLOSSOW, Klin. Monatsbl. f. Augenh. **87:** 230 (Aug.) 1931.

The authors distrust whether dilatation of the pupils might be brought on by voluntary intentions, as they are prompted by emotional factors. They considered two possibilities of the origin of this phenomenon; first, that the sphincter of the pupil may contain striated muscle fibers which receive parasympathetic innervation; secondly, that a complicated intervening process may allow a person to exert a voluntary impulse which would enable him to dilate the pupil at will.

A favorable subject, acting on an intermediary impulse, was found in the person of an oculist, aged 62. He had enjoyed good health, until in recent years sclerosis of the aorta and arteriosclerosis, accompanied by neurasthenic symptoms, developed. Endowed with vivid imagination, this man discovered that his pupils dilated when he imagined that great danger was imminent. He felt no tension of his eye muscles, while other parts of his body felt the effect during these experiments, which were followed by fatigue as soon as the pupils began to contract again.

The pupils dilated from 3 to 4.5 mm. within thirty seconds, during which period the pulse rate increased from 60 to 72 beats, or to 46 beats during the thirty seconds of the experiment. The mydriasis and the concomitant acceleration of the pulse were produced indirectly by action of the sympathetic nerve, via autosuggestion of the sensation of something terrible, a voluntary nightmare. K. L. Stoll.

Physiology

The Behavior of the Light Sense and Ophthalmoscopic Findings in Women with Eclampsia, with Especial Relation to Hepatic Function. A. Santonastaso, Ann. di ottal. e clin. ocul. **60:** 183 (March) 1932.

The author tested the light sense in twenty-five women with eclampsia, using the de Wecker charts and tables V and VI of Masselon, in reduced light, and in certain cases, he used the Foerster adaptometer after one-half hour of dark adaptation. The charts consist in letters offering varying degrees of contrast with a gray background. In twelve cases the light sense was normal or slightly diminished, while in thirteen it was markedly diminished. In some cases tests were repeated during the course of pregnancy, and it was found that during the fifth to eighth months the light sense was normal or showed only moderate reduction for table VI, while in the ninth month a reduction was more constant and reached lower figures. The results of examination in each case are given in detail, including many cases in which tests were made during the attack and were repeated from three days to three years later. Of nine cases examined thirty days after the attack, three showed a marked reduction in light sense, from 1/10 to 2/10 with the de Wecker table, while three showed a moderate reduction, from 1/10 to 6/10 with the table. Two others showed a marked reduction in the light sense with the Foerster instrument. After three months, only one patient showed marked reduction, while after from one and one-half to two years a slight reduction was still present. In some cases with normal records on the photometric tables, the adaptometer recorded a reduced light sense. In a few cases examinations were made in a later pregnancy, and the reduction in light sense was more marked and recovery was slower or incomplete, while pigmentary changes were often present in the periphery of the fundus. In eight cases the hepatic function was tested by the elimination of dye and a retention of dye longer than two hours was always present, while in normal pregnancy it was completely eliminated within this time. Pigmentary changes in the retina were seen in seven of eighteen cases examined, and may be

caused by the angiospasm also observed in these cases. In another group observed some time after eclamptic attacks, pigmentary disturbances were more frequent. Both these and the reduction of the light sense may be caused, in the author's opinion, by abnormal hepatic function. (Bibliography.)

S. R. GIFFORD.

Refraction and Accommodation

ASTIGMATISM BY OBLIQUE INCIDENCE IN THE ACCOMMODATED EYE. A. CUCCHIA, Ann. di ottal. e clin. ocul. **59:** 913 (Nov.-Dec.) 1931.

The author studied the refractions of ten emmetropic eyes, as determined by retinoscopy at angles of 20 and 40° from the visual axis on the nasal and temporal sides with the eye fixing at 5 meters and then at 25 cm. In previous studies of the peripheral and central areas, such as that of Jackson, the angles were not kept constant.

The findings in the resting eyes confirmed those of Lo Cascio, in that there frequently were differences between the nasal and the temporal side of the dioptric system and between the sagittal and the horizontal meridian. Whereas the sagittal meridian at these angles was emmetropic, slightly hyperopic or slightly myopic, the horizontal meridian was, in seven cases, myopic; it was more myopic at the more oblique angles, so that the astigmatism at these angles was "against the rule." It was always greater, sometimes notably so, on the nasal than on the temporal side when measured at the 40° angle, while at the 20° angle the difference was slight.

In eight cases the sagittal meridian was more myopic than the horizontal meridian, the astigmatism being "against the rule," a relation constantly found by Lo Cascio. In two cases, however, the opposite relation obtained. The astigmatism was always greater on the nasal than on the temporal side, when measured at the 40° angle, while at the 20° angle the differences were slight.

In the eye accommodated for 25 cm. (4 diopters), the refractive power at the periphery was always less than at the center. In six cases the difference was from 2 to 3 diopters, while in the others it was less, from 1 to 2.5 diopters in different axes. The difference was greater on the nasal than on the temporal side and was greater in the more peripheral portions. The resulting astigmatism in the periphery varied greatly in different cases, and was, on the whole, much the same as that in the resting eye.

S. R. GIFFORD.

Retina and Optic Nerve

LOCAL RETINAL ARTERIAL HYPERTENSION. C. ESPÍLDORA LUQUE, Arch. de oftal. hispano-am. **31:** 657 (Dec.) 1931.

Local retinal arterial hypertensions are those in which the rise in retinal arterial pressure is brought about by local conditions, such as glaucoma and rhinogenous retrobulbar neuritis, in which it has been mostly studied, other possible ocular causes such as retinal detachment, primary optic nerve atrophy, atrophy secondary to lesions of the chiasm and compression of the optic nerve at the foramen not having been yet explored.

The only cases of glaucoma for the study of this condition are those of chronic glaucoma in which the transparency of the media is preserved. In these, the ocular hypertony affects primarily the venous circulation, and when the intra-ocular tension and the venous tension are equalized there is a spontaneous venous pulse; a further increase of ocular tension equalizes this with the minimum (diastolic) retinal arterial tension with the production of a spontaneous arterial pulse; when this is present the minimum retinal arterial pressure is at least equal to the intra-ocular tension. In glaucoma, when the circulatory disturbance is limited to the venous system, the congestive forms are present; when the arterial circulation is also affected, the ischemic forms result; in both instances the obstruction produced by the increase of intra-ocular pressure is compensated by an increase of the retinal arterial tension, which is merely a defensive reaction (Baillart, Vetter, Duverger and Barré). This retinal hypertension has an absolute value only when the general blood pressure is normal. The preexistence of a general arterial hypertension constitutes a guarantee for glaucomatous eyes, when this precludes the appeal to local mechanisms in order to meet the local increase of intra-ocular tension. The author reports two cases of retinal hypertension with a normal general arterial pressure in which the former was normalized by local operative procedures.

The investigations of Rollet, Sargnon, Colrat and Mounier-Kuhn in cases of rhinogenous retrobulbar neuritis show that, apart from the regular symptoms, an increase in the retinal arterial pressure is frequent, the visual improvement following nasal operations coinciding with a corresponding reduction in the primarily increased retinal arterial pressure.

The investigation of the retinal arterial pressure is also of value in the differential diagnosis of certain more or less obscure cases. In this respect, Espíldora reports a case in which the possibility of an intra-ocular tumor in a monocular glaucoma was eliminated by the finding of a high retinal hypertension in the sound eye. He alsó reports a case in which the diagnosis of embolism was established and a vasomotor spasm eliminated by the finding of a normal retinal pressure. In another case the traumatic origin of a retinitis proliferans was determined by the demonstration of a normal retinal pressure. In still another case, one of paralysis of the sixth nerve after spinal anesthesia with intense headache, an intracranial hypertension was eliminated by the finding of a normal retinal tension.

C. E. FINLAY.

COAT'S EXTERNAL RETINITIS. J. PÉREZ LLORCA, Arch. de oftal. hispano-am. **32**: 349 (July) 1932.

This is the anatomic report of a case diagnosed *intra vitam* as one of retinal glioma, the pathologic examination revealing a total detachment of a retina thickened by a cheeselike exudate on its external surface. Histologic examinations showed the thickened retina and the subretinal exudate infiltrated by disseminated pigment epithelial cells. These were large and round, and were charged with numerous pigment granulations; they were found not only on the external surface of the retina, but also in the thickened external layers.

C. E. FINLAY.

CLINICAL AND ANATOMIC EXAMINATION OF A PATIENT OPERATED ON FOR DETACHMENT OF THE RETINA. M. AMSLER, Klin. Monatsbl. f. Augenh. **87:** 257 (Aug.) 1931.

A patient with a case of so-called spontaneous detachment of the retina had been operated on three times after Gonin's method. New ruptures of the retina formed during the treatment. Two years later the eye had to be enucleated for cyclitis with increased tension. The necessity of exact localization of the rents in the retina for the purpose of reducing the number of operative procedures was stressed by the author, who recommends Arruga's nail. The bisected globe showed a discontinuation of the retina close to the scar caused by the cauterization, apparently due to increased tension. The examination of this globe contributed some light on the problem of the etiology of secondary rents after operative closure of the primary ones. Gonin declared in his discussion that marginal necrosis of the retina will not occur after ignipuncture, as intimated by other ophthalmologists. New tears, in his opinion, will rather form as a consequence of traction of the retinochoroidal scar in an opposite direction to that of the vitreous attached to the edges of the scar. The latter traction will usually appear two weeks after the operation, and is increased by the motion of the eye.

K. L. STOLL.

Tumors

SPONTANEOUS CYST OF THE IRIS. E. A. SHUMWAY, Am. J. Ophth. **14:** 792 (Aug.) 1931.

According to Tertsch, spontaneous cysts are of three types. 1. Those situated in the iris stroma and resulting from cystoid change of endothelial or epithelial cells or serous enlargement of cavities in the stroma. They appear on the anterior surface of the iris. 2. Intra-epithelial cysts arising from the pigmented epithelium of the posterior surface of the iris. They develop backward into the posterior chamber. 3. Cysts due to adhesion of the ciliary processes to the posterior surface of the iris. The author discusses the histology and the various theories of their origin. He reports a case of the first type occurring in a woman of 69, who exhibited a cyst of the ciliary border below, which had torn the iris from its ciliary attachment, displacing the pupil so that it was horizontally oval. Anteriorly it impinged on the cornea, which was clear. The eye was quiet and otherwise normal. The author discusses the various treatments, but did not use them in this case because of the patient's age, the benign nature of the cysts and the presence of an inoperable carcinoma of the rectum.

W. S. REESE.

PRIMARY SARCOMA OF THE CONJUNCTIVAL FORNIX RECURRING AT THE CORNEOSCLERAL JUNCTION. A. RIFFAT, Ann. d'ocul. **169:** 308, 1932.

In a woman of 60 years, among whose antecedents there was no history of cancer, a fusocellular, pigmented sarcoma appeared in the conjunctival sac. A year later the limbus became the site of a recurrence, necessitating enucleation of the eye.

The growth of the tumor of the conjunctiva was remarkable for its rapidity, and for the presence of a number of large irregular nodes. Mitotic figures were frequently seen, showing the tendency to become malignant. The tumor had developed on the conjunctiva, and did not cause either ulceration or epiconjunctival vegetation.

The growth in the limbus was relatively slow, and seemed to be the result of an embolic deposit at the level of the inferior part of the cornea. This tumor developed without pain or metastasis. Certain authors believe that sarcoma of the limbus begins in the cornea, the sclera or the conjunctiva, while Legrange is of the opinion that this disease always has a conjunctival origin, from which it spreads to the cornea and sclera. The tumor started at the limbus of the conjunctiva but did not penetrate the corneoscleral wall. It is known that invasion of this part by sarcoma is very rare. In a case in which the cornea is involved, the sarcomatous tissue appears between Bowman's membrane and the epithelium, raising the latter. Rarely it enters the layers of the cornea and sclera, and attacks the interior of the eye.

S. H. McKee.

Uvea

Significance of Uveal Inflammation. F. A. Kiehle, Northwest Med. **31:** 226 (May) 1932.

According to Kiehle, the significance of uveal inflammation lies in the possible far-reaching and serious consequences of ciliary congestion. Continued or repeated dilation of the vessels in this highly vascular area results in alterations in the vessel walls and consequent changes in the dialyzed fluids. This alteration in the nutritive elements supplied the lens and the anterior segment of the eye, in turn, necessarily produces changes in their structure and in the manner in which they perform their function. The region of the limbus is so constructed that it may yield readily to intra-ocular pressure with resultant change in the refraction of the eye. When the scleral tissue fails to yield to this pressure, the effect is registered in various symptoms of asthenopia. The causes of ciliary congestion are doubtless exceedingly numerous, and as yet no satisfactory classification has been established. It is possible that the causes are so complex as not to lend themselves to any simplified grouping. Serious consequences from inflammation of this region are easily possible, so that painstaking study is demanded. In this study, the slit-lamp has been found to be of great assistance. [J. A. M. A.]

Detachment of the Choroid Nine Months After Cataract Extraction, with Operative Reattachment: Report of a Case. W. Loehlein, Klin. Monatsbl. f. Augenh. **87:** 825 (Dec.) 1931.

A man, aged 68, was operated on successfully for cataract nine months previously. Three days before the examination he noticed a deterioration of vision which had been 5/6 up to that time. Examination revealed detachment of the retina and choroid in three globular, firmly extended portions in the lower temporal and nasal part of the

fundus, with vision of only 1/10. The eye was soft and the anterior chamber narrow; a constant epiphora existed, although the eye was completely free from congestion. The fluorescein test showed a leaking spot in the corneal scar, which apparently had been reopened by some mechanical insult although the patient knew of no injury. Cauterization of the entire scar produced closure of the fistula, so that tension was again nearly normal four days later. The choroid had become reattached a week after cauterization, bringing vision up to 5/10; this increased to 5/7 later, on restitution of the visual field for white and colors.

A similar case occurred in a patient with epiphora who had been treated for conjunctivitis elsewhere for several months. Loehlein discovered the fistula and the detachment of the choroid.

K. L. Stoll.

Visual Tracts and Fields

The Value of Quadrant Field Defects in the Localization of Temporal Lobe Tumors. D. Kravitz, Am. J. Ophth. **14:** 781 (Aug.) 1931.

The author briefly discusses the rôle of the ophthalmologist in the diagnosis of lesions of the brain, especially those of the temporal lobe. The case is reported of a man, aged 26, who had been having attacks of unconsciousness for one year. These lasted a few seconds and were accompanied by visual or auditory auras. For the past month he had had diplopia. He had had two attacks of rhinorrhea and headache, the last being accompanied by blurred vision. Physical examination gave negative results except for the eyes, which revealed a bilateral papilledema of about 1.5 diopters in the right eye and 2.5 diopters in the left. There was homonymous diplopia, which was the same in all fields but increased for distance. There was no diplopia at the reading distance. Perimetry revealed an homonymous hemianopia of the upper left quadrant. Dandy removed a large deep-seated glioma and with it practically the entire right temporal lobe of the brain. On regaining consciousness the patient noticed absence of diplopia, but marked hypertonia and jacksonian attacks of the left side developed. The papilledema disappeared.

W. S. Reese.

Variations of the Normal Blind Spot with Special Reference to the Formation of a Diagnostic Scale. H. W. Wentworth, Am. J. Ophth. **14:** 889 (Sept.) 1931.

This technical article does not lend itself to abstracting. It is a study of the blind spots of two hundred normal persons. The Ferree-Rand perimeter was used and the test object carried from the center of the blind spot outward, from 16 to 24 points being charted. A white disk, 5.8 mm. in diameter, was used as a test object and the screen placed 33 cm. from the eye. Illumination was kept constant at 7 foot-candles. The average size of the blind spot was found to be 11.4 sq. cm., the extremes being 6.8 sq. cm. and 17.5 sq. cm. This average size increased with age. As a standard for diagnostic comparison the distribution

curve was regarded as more important than the average size. A number of tables and charts are given. This article should be read to be fully appreciated.

W. S. REESE.

CORTICAL LOCALIZATION OF THE MACULA IN MAN. MANUEL BOLADO and JORGE MALBRAN, Arch. de oftal. de Buenos Aires **7**: 159 (May) 1932.

After reference to the classic localization of the macula in the apex of the occipital lobe and to the extreme paucity of pathologic data in reported cases of central scotoma (involving the fixation point, with preservation of the remainder of the visual field), the author criticizes three cases mentioned by Wilbrand and Sänger. After a summary review of the more recently reported cases he points out that the great majority of the cases reported have only a clinical foundation.

In connection with his case, he discards the usual anatomic nomenclature, making use of the cyto-architectonic fields of the occipital lobe according to Kleist and von Economo, who described along the calcarine fissure a striate zone (Genari's stria), with superimposed parastriate and peristriate zones.

A case is reported with detailed clinical and pathologic findings. There was a pure central scotoma due to a lesion limited to the apex of the occipital lobe apparently of operative origin. A subsequent excision of the apex of the occipital lobe with the radium knife was immediately followed by a homonymous hemianopia, the limiting line passing through the fixation point. After a few days the limiting line passed outside this, with persistence of an independent central scotoma, the lesion involving the peripheral field.

Histologic examination of the excised cortex showed that the operation had affected the striate and parastriate zones. From this it is seen that a cortical lesion of the apex of the occipital lobe was immediately followed by a homonymous hemianopia passing through the fixation point, the functional disturbances not being limited to this point but also affecting the peripheral visual fields. Later, however, the defect of the visual field respects the fixation point, the limiting line passing outside, which disagrees with classic ophthalmologic teaching, according to which a permanent central scotoma should have persisted.

The author concludes that the central scotomas described in the clinical cases hitherto reported were due to lesions of the optic tract in traumatic cases; with the lesion in the occipital lobe, a coexisting base fracture with secondary lesion of the optic tract usually cannot be excluded. Of the three cases reported by Wilbrand and Sänger, in two no histologic examination of the optic tracts was made; in the other one (Nonne's), such a lesion was reported. The double macular projection (Lenz and Monakow) explains how an isolated lesion of the apex of one occipital lobe cannot produce a persistent central scotoma.

Incidentally, the author calls attention to the value of quantitative perimetry, which is fully illustrated in the study of this case.

C. E. FINLAY.

DISTURBANCES OF THE FIELD OF VISION CAUSED BY HIGH BLOOD PRESSURE: REPORT OF TWO CASES. E. KLAUBER, Klin. Monatsbl. f. Augenh. **87:** 401 (Sept.) 1931.

The first case concerns a woman, aged 40, in whom periodic central scotomas occurred alternatingly in both eyes for twelve years. After curettage of the ethmoidal cells had produced only slight improvement, constitutional arterial hypertony was found to be the cause of the attacks of scotoma. The fundus showed narrow arteries and Gunn's crossings. Transient venous hemorrhages were noticed in the retina after internal application of sodium nitrite. Disturbances of the circulation, caused by protracted vascular crises, produced the reversible dysfunction of the maculas. At the time of the publication, the attacks of scotoma had disappeared with use of a fruit diet, treatment for constipation and cold baths.

In the second case, a woman, aged 51, had blood pressure of 240, due to nephrosclerosis. Her fields of vision showed contraction of the entire periphery and absolute wing-shaped scotomas, which extended from the blind spot and were identical in both eyes. Extensive Gunn's crossings and tortuous narrow vessels were present. The scotomas around the blind spot, so-called "*Gefaessbaumskotome*," are due to pressure on the retinal tissue by hypertony in the large vascular trunk of the retina.

K. L. STOLL.

Sympathetic Ophthalmia

PRECOCIOUS SYMPTOMS OF SYMPATHETIC OPHTHALMIA. CARLOS DAMEL, Arch. de oftal. de Buenos Aires **7:** 133 (March) 1932.

The author refers to five cases reported by Vogt, and to two reported later by Jeandelize, of precocious sympathetic ophthalmia. The disease was distinguishable solely by biomicroscopy. By this method there were seen fine dotlike and starlike precipitates, with a few cells on the posterior corneal surface, bright specks floating in the aqueous or lying on the anterior lens capsule in a fine dustlike form, and abundant white and reddish-white spots in the vitreous. There was little or no reduction in sight. The author reports a case of his own in which after extraction of a cataract, followed by an iridocyclitis with some hypopyon, conditions similar to those described were noticed. Vision was normal and the Wassermann reaction negative. Enucleation of the eye operated on, with a subsequent mercurial treatment, was followed by a gradual improvement in the sympathizing eye.

C. E. FINLAY.

Therapeutics

DIVERSIFIED THERMOPHORE THERAPY. L. T. POST, Am. J. Ophth. **14:** 752 (Aug.) 1931.

The author describes the thermophore, and the method of using it. The thermal death points of the different ocular tissues are given. Reference is made to the palliatively successful use of the thermophore in

glaucoma and the complete success following its application to a sarcoma of the iris. Its use in ulcers, keratitis and various other conditions is discussed.

W. S. REESE.

ROENTGEN THERAPY IN PITUITARY TUMORS. G. E. PFAHLER and E. W. SPACKMAN, Am. J. Ophth. **14:** 796 (Aug.) 1931.

Roentgenotherapy of the pituitary gland is discussed, especially as to its relief of headache and ocular symptoms. The latter can best be judged by perimetry. Systemic improvement is also noted. In cases exhibiting the ophthalmic or chiasmatic syndrome, treatment is uncertain. The radiosensitivity of pituitary tumors and the technic of irradiation are discussed and six cases reported. The following conclusions are drawn: 1. Good results in the treatment of pituitary tumors have been reported by at least seventy-seven authors, but the successful cases do not respond equally. 2. The solid adenomas usually respond. The cystic adenomas do not respond to this treatment. An endothelioma has been successfully treated. Some tumors that have not responded have been found to be carcinoma or sarcoma. 3. The surgical statistics seem to show permanent recovery in 20 per cent, while 80 per cent of the cases are followed by recurrent symptoms. Heuer's statistics show 20 per cent of the tumors operated on to have been cystic adenomas. It seems that cystic adenomas are responsive to surgery and the solid adenomas are responsive to irradiation. 4. Since surgery involves great risks, and since irradiation shows no mortality and in skilful hands should involve no damage, it would seem advisable to treat with the high voltage x-rays first, keep the patient under observation for from six weeks to six months and operate if there is insufficient response to irradiation.

An extensive bibliography is appended.

W. S. REESE.

GRENZSTRAHL THERAPY OF ACUTE AND CHRONIC CATARRHAL CONJUNCTIVITIS, ILONA KRASSŌ, Ztschr. f. Augenh. 75:285 (Nov.) 1931.

By means of careful experimental and clinical research on the eyes of rabbits and man, Krassō was able to demonstrate the relative harmlessness of the *Grenzenstrahlen* (border rays) that are described as lying in the spectrum of electromagnetic oscillation between the roentgen and ultraviolet rays. A technic for the use of this therapy in conjunctival infections is given. Sixteen patients with acute catarrhal conjunctivitis were treated with one exposure of light. In thirteen, the acute inflammation was shortened considerably and favorable results were obtained. In a group of thirteen patients with chronic conjunctivitis having pathogenic organisms in the secretion, it was possible to relieve eleven of them of their distressing symptoms. In persons with chronic conjunctivitis exposed to the irradiation, it was observed that discomfort was eradicated; secretion, hyperemia and edema decreased but hypertrophy remained. Recovery was rapid when the disease was treated early. Krassō advocates the use of this therapy in chronic dacryocystitis, chalazia and milia of the conjunctiva.

A. M. YUDKIN.

CLINICAL TREATMENT OF ULCUS SERPENS. JOSEF BLAICKNER, Ztschr. f. Augenh. **75:** 304 (Nov.) 1931.

The pneumococcus type IV is the most frequent cause of ulcus serpens of the cornea. No single procedure has been found to eradicate the invading organism and repair the destruction. It is necessary to remove all possible sources of infection. If the tear sac is inflamed, it is best to extirpate it. When the lesion is small and superficial, it is treated with a fresh solution of 1 per cent ethylhydrocupreine hydrochloride and mercurial salves. Should a small round accumulation of purulent material be present in the superficial ulcer, a red hot cautery is applied to the lowermost portion of the accumulation in the cornea, so that the area may drain and the tissue be made more accessible to medication. Frequently within two days after treatment with ethylhydrocupreine hydrochloride, the cauterized area exfoliates a membranous and shredlike degenerated tissue. The ulcer is inundated by using a 1 per cent solution of ethylhydrocupreine hydrochloride every two hours, night and day, supplemented with an ethylhydrocupreine hydrochloride salve. In extensive ulceration, with increased intra-ocular pressure and a hypopyon occupying from one half to one third of the anterior chamber, a broad paracentesis of the cornea at the limbus is made with a keratome. The eye should not be bandaged. The patient is put to bed and kept there until the lesion epithelizes. The author attributes the favorable response to the formation of a bacterolysine, which in turn checks the further pneumococcus invasion. He prefers the use of the combination of ethylhydrocupreine hydrochloride and oxycyanide to the separate solutions of the drugs. A perforation of the cornea should be avoided.

A. M. YUDKIN.

TREATMENT OF BLEPHARITIS WITH MALACHITE GREEN. A. V. ALEEVA, Russk. j. oftal. **13:** 420 (April) 1931.

The author reviews the literature on the treatment of blepharitis by aniline dyes. Since brilliant green was not obtainable, he used malachite green. Twenty patients suffering from blepharitis varying in severity of the process and in duration were treated with malachite green for from one to two months. Five of these patients had recurrent blepharitis which improved rapidly after repeated treatment.

The author recommends the treatment of blepharitis with aniline dye highly because of the simplicity of its use and because of the favorable results obtained in severe cases.

O. SITCHEVSKA.

Society Transactions

EDITED BY DR. JOHN HERBERT WAITE

AMERICAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

PARKER HEATH, M.D., *Secretary*

Eighty-Third Annual Session, New Orleans, May 9 to 13, 1932

HARRY FRIEDENWALD, M.D., *Chairman*

THE RESECTION OPERATION FOR STRABISMUS. DR. CONRAD BERENS, New York.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, September, 1932, p. 321.

THE REACTION TIME OF THE NORMAL PUPIL. DR. H. S. GRADLE and DR. WALTER ACKERMAN, Chicago.

This paper appeared in full with the discussion in *The Journal of the American Medical Association,* Oct. 15, 1932, p. 1334.

A SYNDROME IN UVEAL TUBERCULOSIS. DR. WILLIAM C. FINNOFF, Denver.

This paper will be published in full with the discussion in a later issue of the ARCHIVES OF OPHTHALMOLOGY.

SIGNIFICANCE OF CHOROIDAL HEMORRHAGE. DR. ARTHUR J. BEDELL, Albany, N. Y.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, August, 1932, p. 186.

URINARY PROTEOSE IN OCULAR ALLERGY. DR. LLOYD MILLS and DR. GEORGE MARTYN, Los Angeles.

Between 40 and 60 per cent of all persons have an idiosyncrasy to one or more foreign substances touched, inhaled or swallowed by them. This characteristic susceptibility is inherited in about half, is increased by constant or repeated contacts, and is exaggerated so greatly by concentration of the material which provokes the disturbance that all persons may be considered as potentially sensitizable to such substances. Hypersensitiveness to ingested food appears in connection with insufficiency of digestive ferments, bacterial and amebic intestinal infections, defective function of the liver and congenital insufficiency of the endocrine-autonomic system. Bacteria produce their allergic effects on the body partly by means of the toxins which they produce and in some measure by the destruction of the protein tissues of their host.

The sensitization of the skin and mucous membranes is the measure of all allergy, for it provides a means of testing sensitization to antigen

by intradermal injection, and also gives an index of the strength of solution of the desensitizing antigen.

The type and course of the allergic reactions are dependent on the antigen and vary according to the localization of the antibodies. When this reaction occurs within closed chambers, like the joints, the skull (pia mater), the eye, obstructed nasal sinuses or the ears, pain may become an essential part of the reaction, depending on the degree of tension.

Barber and Oriel, in their work on asthma and its allied allergies, found that the urine contained a proteose-like body which was greatly increased during the attacks. A reaction was produced by the intradermal injection of this "proteose" into a sensitized person identical with that seen on the injection of an antigen to which an allergic person is sensitized. A definite parallelism was found between the increased amino-acid content of the blood in the active allergic stage and the increased proteose content of the urine and its toxicity, increases attributed to the greater breakdown of tissue. It has been proved that (*a*) An asthmatic patient gives, in a large number of cases, a positive skin reaction to his own proteose by dermal, intradermal and "patch" tests. (*b*) This sensitivity can be transferred to a normal man by the injection of a sensitized patient's serum. A positive Prausnitz-Küstner reaction is obtained when a dilute solution of proteose from the urine of the allergic patient subsequently is injected. (*c*) The proteose obtained from a patient suffering from serum-sickness gives a positive reaction when injected in very small quantities into a known "horse asthmatic," and one patient with horse asthma will react to the proteose from another patient with horse asthma. (*d*) A specific antigen from milk or egg can be identified in the urinary proteose of milk-sensitive or egg-sensitive patients, proving beyond reasonable doubt that the urinary proteose in sensitization contains the antigen to which the patient is sensitized. (*e*) The production, by the liver, of a fresh substance (secondary antigen) from the original antigen, as the experiments of Manwaring and co-workers prove may occur, explains why attempts to desensitize with the original antigen, in cases in which this is known, are not always successful. A further explanation of the specificity of the treatment with autogenous "proteose" is given by Oriel's statement that the original antigen not only has been demonstrated in the urinary proteose but that in multiple sensitizations the autogenous "proteose" probably contains a mixture of the original antigens together with the corresponding secondary antigens. (*f*) "In specific food sensitization it has been possible to sensitize guinea-pigs actively to foods to which the patient was sensitized, using the urinary nitrogenous substance from that patient as the sensitizing dose" (Oriel). (*g*) The specificity of urinary proteose finally is confirmed by marked exacerbations of the original lesions and symptoms if excessive dosage is used.

The original solution of proteose, called 1 : 1,000, is used in dermatologic testing and desensitization in the further dilutions of 1 : 10,000, 1 : 100,000, 1 : 1,000,000, 1 : 100,000,000 and 1 : 1,000,000,000. Subcutaneous injections, beginning with a minimal dose, are given every three to five days in slightly increasing doses. The best results are apparent when the dosage is held below the point of a general reaction. Reactions usually occur on the third day after injection, if at all.

The following conclusions were made:

1. The clinical improvement which has followed this first use of autogenous urinary "proteose" in forty-one of forty-four cases of disabling chronic ocular disease of obscure origin is evidence of the allergic origins of such conditions.

2. The ocular reactions resulting from a relatively excessive dosage of autogenous urinary "proteose" in these cases are conclusive evidence of the specificity of this "proteose."

3. The degree of improvement in these extreme cases of ocular disease justifies the extension of this investigation to ocular disease of otherwise indeterminable origin, but known to be progressive in type, at their earliest recognizable stages.

(This paper will appear in full with the discussion in the *Transactions of the Section on Ophthalmology, American Medical Association.*)

DISCUSSION

DR. RICHARD W. WHITEHEAD, Denver: Our clinical and experimental studies on the urinary proteose described by Drs. Baker and Oriel of Guy's Hospital, London, were begun in the fall of 1930. The clinical studies have been directed toward the investigation of the therapeutic value of injections of proteose in the treatment of patients with frankly allergic conditions met with in general medicine, such as asthma, hay fever, eczema, urticaria, migraine and arthritis. Our results in many of these conditions have been encouraging, and in general they have been corroborative of those reported by the investigators at Guy's Hospital.

We cannot fail to emphasize anew the fact mentioned by Drs. Mills and Martyn that the general treatment of these patients is highly important. Removal of foci of infection and careful attention to the nutritive requirements of the patient are essential to success with proteose therapy. It has been our experience that proteose therapy will often make a latent focus of infection manifest itself, and that further treatment with proteose should be preceded by the eradication of this focus.

Results in our animal experiments likewise favor the specificity of urinary proteose. Animals sensitized to a primary allergen (dog serum) show evidences of an anaphylactic response following the injection of proteose from an asthmatic person sensitive to dogs. The animals show no signs of anaphylaxis when another proteose is injected which was obtained from an asthmatic person insensitive to dogs.

DR. GEORGE PINESS, Los Angeles: In these forty-four cases reported, of which only ten are published, there is no evidence that there is an allergic background. It is my experience that the background of allergy is always present. People are born sensitive and are free until such time as the threshold is broken down, and then symptoms may arise. Race, sex, creed, color and environment are not factors in the production of allergy. In this group of cases no evidence is produced that skin tests of any variety were made—negative or positive. Skin tests do not make the diagnosis. The man who knows allergy, whether of the eye, ear, nose or throat, does not require a skin test to make a diagnosis; but it is used as an adjunct to confirm his diagnosis.

DR. LAURA A. LANE, Minneapolis: Proteoses are more complex than the completely hydrolized amino-acids. The higher proteoses are toxic; they inhibit the coagulation of the blood and can cause febrile disturbances and mild inflammatory reactions, and even death, in experimental animals. The first products of protein hydrolysis are the most toxic.

Proteoses have little power to stimulate antibody formation. When proteoses are produced in considerable amounts by autolysis of pathologic tissues they appear in the urine and their presence is of diagnostic importance. Whipple has described highly toxic proteoses from the contents of closed intestinal loops. The intestinal wall has the power to change proteose into amino-acids, but the liver does not have this property, and small amounts of proteose introduced into the portal vein will cause albuminosuria.

The problem of allergy is most important to the ophthalmologist. Rowe found that 71 per cent of his patients gave a positive family history of allergy. Vaughn and Duke likewise corroborate this hereditary factor. It is probable that the tendency to become sensitive is inherited, according to Mendel's law. The intermittent taking of unusual foods, as well as the excessive intake of certain kinds of food, may precipitate allergic attacks. About 40 per cent of all food allergies are due to wheat, a significant fact since it is one of the most largely consumed foodstuffs and contains considerable carbohydrate and protein.

DR. ALAN C. WOODS, Baltimore: The authors apparently lay great stress on the action of histamine. People who have been investigating for a long time in this line have been searching and studying extreme anaphylactic shock. Dalrymple and his co-workers have been working with histamine and have been able to show clearly that histamine in animals gives symptoms of anaphylactic shock. They point out that the sensitized muscle in the guinea-pig, which has been completely desensitized by the action of a specific serum, will still react to histamine. And they point out that the symptoms are much like traumatic shock.

DR. GEORGE MARTYN: Early in our work with the eye it was evident that we were dealing with two clinical forms of the allergic process which at times were combined. Eyes having acute inflammatory reactions of the external or internal coats nearly always were found to have a primary bacterial antigen as their probable source. It was a novel experience, accustomed as we had become to treating corneal ulcers by cautery or pasteurization, to see fresh and increasing crops of typical ulcers fade within twenty-four hours after the sole use of staphylococcic vaccine intradermally.

It is still the custom to class all cases of massive exudate of the vitreous, without discoverable cause, as tuberculous. Our first case shows, however, that this condition may be merely a severe allergic result, and as such, fully responsive to autogenous proteose alone.

The advantage of autogenous proteose over all nonspecific proteins is that when one uses proteose one gives a measured quantity of the specific excitant of that body. Nonspecific proteins have their definite virtue in that they cause the liver to produce proteose in greater or lesser quantities. If enough is created to neutralize the antibodies, cure results; if too much is formed, an accentuation of all symptoms with

redeposit of antibodies is obtained. With nonspecific proteins one deals with unknown quantities throughout, while with autogenous proteose a definite dosage is employed to produce a definite effect.

GYRATE ATROPHY OF THE CHOROID AND RETINA (FUCHS). DR. HUNTER H. MCGUIRE, Winchester, Va.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, September, 1932, p. 372.

ANGIOID STREAKS OF THE RETINA AND PSEUDOXANTHOMA ELASTICUM. DR. GRADY CLAY, Atlanta, Ga.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, September, 1932, p. 334.

THE BIOCHEMISTRY OF THE LENS: I. THE PERMEABILITY OF THE CAPSULE OF THE LENS. DR. SANFORD R. GIFFORD, DR. JAMES E. LEBENSOHN and MR. IRVING S. PUNTENNY, Chicago.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, September, 1932, p. 414.

FOREIGN PROTEINS AND GOLD IN THE TREATMENT OF UVEITIS. DR. WILLIAM L. BENEDICT and DR. WILLIAM H. GOECKERMANN, Rochester, Minn.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, August, 1932, p. 250.

ABERRATIONS OF EYES AND LENSES. DR. EDWARD JACKSON, Denver.

This paper appeared in full with the discussion in *The Journal of the American Medical Association,* Aug. 6, 1932, p. 437.

METASTATIC CARCINOMA OF THE OPTIC DISK: WITH REPORT OF A CASE. DR. WILLIAM THORNWALL DAVIS, Washington, D. C.

This paper appeared in full with the discussion in the ARCHIVES OF OPHTHALMOLOGY, August, 1932, p. 226.

SARCOMA OF THE CHOROID: HISTORY OF SIX CASES, WITH EARLY OPERATION. DR. H. MOULTON and DR. E. C. MOULTON, Fort Smith, Ark.

This paper appeared in full with the discussion in *The Journal of the American Medical Association,* Aug. 6, 1932, p. 460.

UVEAL PIGMENT: HYPERSENSITIVITY AND THERAPEUSIS. DR. ALAN C. WOODS and DR. MILTON F. LITTLE, Baltimore.

This paper appears in full in this issue of the ARCHIVES OF OPHTHALMOLOGY, p. 200.

INEXPERT REFRACTION. DR. JOHN GREEN AND DR. CARL BEISBARTH, St. Louis.

This paper appeared in full with the discussion in *The Journal of the American Medical Association,* July 9, 1932, p. 101.

ASTHENOPIA: A PSYCHONEUROSIS AND A MEDICAL RESPONSIBILITY. DR. C. W. RUTHERFORD, Iowa City.

This paper with the discussion appeared in full in *The Journal of the American Medical Association,* July 23, 1932, p. 284.

THE BASAL METABOLIC RATE IN PROGRESSIVE AXIAL MYOPIA. DR. LOUIS BOTHMAN, Chicago.

The progress of the myopia was measured in thirty-eight patients by repeated refractions with atropine. Special care was taken to eliminate all eyes that had any evidence of ocular or sinus disease, and no patient studied had more than 3 diopters of myopia when first seen. All patients were under 20 years of age, and only seven were over 15 years old. In my first series, five patients were more than 15 years of age. The patients in cases 6 and 16 were reexamined for evidence of sinus disease because the myopia progressed in only one eye. Turner stressed sinus disease as the cause of unilateral myopia.

A study of the table reveals that there were thirteen males and twenty-five females, a ratio of almost 1:2, while in my first series there were ten males and twenty females. In these unselected groups the incidence of myopia was: males, twenty-three and females, forty-five—a 1:2 ratio. The ages were from 8 to 19, the average being 12.8 years. The average weight was 43.2 Kg., and the average height 148.2 cm. The increase of myopia showed a wide range, there being no increase in the left eye in case 6 and in the right eye in case 16, while the greatest increase was 4.25 diopters in the right eye in case 1. The average increase was 1.39 diopters.

The basal metabolic rates varied greatly. Case 21 showed the highest rate, minus 7 per cent, and case 4 the lowest, minus 36 per cent. The average rate was minus 19.3 per cent.

It has been extremely rare to find a case of progressive myopia with a plus rate without hyperthyroid symptoms. There was one case (case 10) in the first series. The myopia has usually been stationary in cases showing plus metabolic rates. The patient in case 5 had a plus 12 per cent rate at the age of 12 when he had returned from a summer camp. I have no rate that was taken before that time. His myopia had increased 0.75 diopter in eighteen months. The next year, he had an increase of 0.25 diopter in the right eye and 0.50 diopter in the left, and his rate was minus 19 per cent. He has not been on treatment.

That the thyroid deficiency may be a factor in this myopic group is supported by the facts that most of the patients were overweight for their age and height, and that many underweight patients with low rates gained while taking thyroid. Several patients whose myopia had ceased to progress had plus rates, and the only hyperopic member of one family of six under observation was a son with exophthalmic goiter. Another patient had progressive myopia (final reading, 6 diopters) until an exophthalmic goiter developed, which was removed. His myopia has been stationary for the past eight years.

In treatment I use 1½ grains (0.097 Gm.) of thyroid extract daily, increasing the dose if the basal metabolic rate remains too low and decreasing it if any toxic symptoms appear.

(This paper will appear in full with the discussion in the *Transactions of the Section of Ophthalmology, American Medical Association.*)

DISCUSSION

Dr. W. R. Buffington, New Orleans: Many thousands of tests must be made by various observers, both in myopic and nonmyopic children, before a true estimate can be made of the relationship between myopia and hypodysfunction of the thyroid.

In addition, serious thought should be given to the biochemical abnormalities and reactions in progressive myopia. Calcium deficiency, which in turn may be an endocrine disturbance, is often present. Whether it is a causative agent must also be settled by future study. If oculists are to play an important part in the prevention and arrest of progressive myopia, due consideration must be given to heredity, environment, posture of the growing school child, biochemistry and, finally, to a comprehensive study of endocrine disturbances.

Dr. Meyer Weiner, St. Louis: I have the record of the basal metabolism rate of 112 cases of progressive myopia. Of these cases 12 registered zero, 18 registered plus and 82 registered minus. Of those registering minus, 4 were minus 30 or above; 16 between 20 and 30; 36 between 10 and 20, and 26 below 10. Most of the children were well nourished, or inclined to be fat.

Pathogenesis of Retinitis Pigmentosa: With a Note on the Phagocytic Activity of Müller's Fibers. Dr. Jonas S. Friedenwald and Dr. Eugene Chan, Baltimore.

This paper appeared in full with the discussion in the Archives of Ophthalmology, August, 1932, p. 173.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Algernon B. Reese, M.D., *Secretary*

April 18, 1932

Mark J. Schoenberg, M.D., *Chairman*

Unilateral Exophthalmos in Intracranial Tumors with Special Reference to Its Occurrence in the Meningiomas. Dr. Charles A. Elsberg, Dr. Clarence C. Hare and Dr. Cornelius G. Dyke.

In a series of 807 cases of verified intracranial neoplasm, marked protrusion of one eyeball occurred in fifteen patients or in 1.9 per cent. The frequency with which meningeal growths with cranial hyperostoses of the anterior part of the skull cause a marked protrusion of the eyeball is so great that one is apt to think only of a meningioma when a case of this kind is seen. In the fifteen cases of the series, ten patients were found to have meningiomas; one had a primary adenocarcinoma of the scalp and skull, one an epidermoid, one Paget's disease and two orbitoethmoidal osteomas.

The protrusion of the eyeball was on the left side in nine, and on the right side in six of the fifteen patients. In seven of eight females

the exophthalmos was on the left side, and in five of seven males it was on the right side. This frequency of left-sided lesions in women and of right-sided lesions in men was also found in the cases reported in the literature by others.

The protrusion of the eyeball was most often due to direct perforation of the tumor into the orbital cavity, thickening of the orbital walls or direct extension of the growth through an enlarged superior orbital fissure. In some cases the mechanism which produced the protrusion of the eyeball may have been an increase of pressure in the middle cranial fossa directly transmitted to the orbital contents through the superior orbital fissure.

The eyeball was most often pushed forward, downward and outward. In most of the patients, the movements of the affected eyeball were limited in all directions, but the limitation was not always directly proportionate to the degree of protrusion.

The vision of the affected eye was well preserved in six of the patients; there were some diminution of vision in five patients, marked diminution in three and complete loss of vision in the affected eye in one. In most instances, the fields of vision were normal in shape and size; in a few there were large scotomas; in three there was a temporal defect on the affected side. The fundus changes varied within wide limits. On the side of the lesion, the margins of the disk were sometimes definitely blurred and indistinct, while the fundus of the other eye showed nothing abnormal. In some of the patients, the affected eye showed a primary optic atrophy. If there was a papilledema, it was found in both eyegrounds as an evidence of a general rise of intracranial pressure. Unless there was a papilledema, distinct congestion of the veins of the retina of the affected eye was rarely observed. This absence of evidences of stasis in the retinal veins was surprising, and led the authors to conclude that the exophthalmos was not due to venous stasis in the orbit and was not, in any of the patients, the result of compression of the cavernous sinus or the ophthalmic vein.

For a period of years, unilateral exophthalmos may be the only sign of a serious intracranial lesion, and there is often a long delay before the real cause is recognized and the patient is referred to the surgeon. In the absence of demonstrable disease in the orbit or the adjacent air sinuses, a slowly progressive unilateral exophthalmos may be, therefore, an important sign of an expanding intracranial lesion. It is not at all necessary that other symptoms or signs of a tumor of the brain are present.

DISCUSSION

DR. CORNELIUS G. DYKE: It is my purpose to review a few of the findings from the roentgenologist's standpoint, and to stress a few of the landmarks of the skull that are commonly affected by this group of tumors which produce unilateral exophthalmos. The films of ten of the fifteen patients are available for study. In this group there are six meningiomas, two orbito-ethmoidal osteomas, one adenocarcinoma of the scalp and skull and one epidermoid. In going over the films of these ten cases, it was found that in seven there was evidence of increased intracranial pressure. This was produced by the six meningiomas and the one adenocarcinoma of the scalp. In other words, the other two

types of tumors, the one epidermoid and the two orbito-ethmoidal osteomas, produced no evidence of increased intracranial pressure.

We have found that a diagnosis of an extrasellar tumor can be made by comparing the proportional degree of atrophy of the posterior clinoids and dorsum with the atrophy in the floor of the sella. In extrasellar tumors the posterior clinoid processes and dorsum sellae are relatively more atrophic than the floor of the sella turcica.

Calcification was seen in only one of the patients in this series, and this was in a very large meningioma extensively involving the left middle fossa. In all of the ten cases in which we were able to review the films, there was involvement of the walls of the orbital cavity, which we believe accounted for the exophthalmos.

The superior orbital fissure was definitely involved in five cases. In three it was changed as the result of bone absorption or destruction, and in the other two cases there was a definite thickening of the walls owing to new bone formation. In all five cases the neoplasm that produced these changes was a meningioma.

A study of the films shows that the posterior and superior portions of the orbital cavity are most frequently encroached on by these tumors. This was to be expected because of the involvement of the orbital surface of the frontal bone and of the sphenoid bone. The tumors that produce unilateral exophthalmos involve the greater and lesser wings of the sphenoid bone or the orbital plate of the frontal bone, or both, and it is this particular part of the skull which must be carefully scrutinized.

Osteomas arising in the cranial cavity are infrequent, and form less than 0.5 per cent of all intracranial tumors. As seen on the roentgenograms, they are of two types: a cauliflower-like growth with many areas of decreased density within it and ivory-like tumors. These tumors also have a predilection for certain areas in the skull, one being the anterior and medial end of the petrous region and the other the junction of the cribriform plate and the orbital surface of the frontal bone. When they occur in the latter position, they must be differentiated from the hyperostoses produced by the meningiomas.

The epidermoids are rare intracranial tumors. Only ninety or so have been reported in the literature. I wish to call attention to the sharp, cleancut appearance of the defect in this tumor, in contrast to the irregular circular defect that was produced by the meningioma. It is unusual for a meningioma to produce a definite defect in the skull, and one should be quite hesitant to diagnose it as such when a defect in the bone exists.

In summary, when a patient with unilateral exophthalmos is examined, a careful stereoscopic study of the orbital plate of the frontal bone and of the lesser and greater wings of the sphenoid bone should be made. In six of the patients studied, the orbital plate of the frontal bone was involved, and in seven either the lesser or greater wings of the sphenoid bone.

A Case of Bilateral Lindau's Disease. Dr. Ralph I. Lloyd.

Miss M. M., aged 16, came to the Brooklyn Eye and Ear Hospital during January, 1931, to get a glass to improve the vision of the left eye, which was 1/60. No other complaint was made, and no date when

the fading vision began could be assigned. There were two large and tortuous vessels running from the left disk along the route of the usual superior temporal vessels. It was difficult to say which was artery and which was vein. The inferior temporal vein was involved throughout in the same way and the stalk of the superior nasal vein was also swollen for about 2 disk-diameters above the papilla. The entire circumpapillary region was white to and beyond the macular area. Next beyond this was a zone of small white flecks, and all of this change was in the deep portion of the retina or in the choroid. There are no hemorrhages anywhere. Just above the superior temporal vessels and opposite the macula there was a typical cyst with an enlarged artery entering it.

The right eye had not caused the patient to complain until recently, when the vision diminished to 3/10, coincident with changes in the macular area. This eye was at first considered normal, but a typical cyst was later found just external to and slightly above the macular area. The vessels connected therewith were but little larger than normal, but they had recently doubled in size. Six months after her first visit, a number of white flecks appeared just between the node and the macula. For a time this did not affect the vision, but recently the vision has been failing, with enlargement of the node, increased tortuosity of the vein and an increase of the exudate. Now there was a typical half "star figure," limited internally by the vertical meridian. The slit-lamp also showed some new fibrin on the posterior corneal surface.

The unusual fundus picture attracted attention at once, and she was referred to Dr. John Evans for a thorough examination. Urinalysis and the Wassermann and other tests gave negative results. Roentgenograms disclosed an odd shadow in the region of the spleen, but no cerebral defects have been found, as might have been expected from the histories of similar cases.

There are other children in the family but no similar case has been found. The case history is quite like those of other cases of von Hippel's disease in the literature, but differs from those cases recently described by Lindau which were featured by similar vascular lesions in the cerebellum and occasionally in the pancreas, stomach or renal pelvis. Patients with naevus flammeus of the face often have angiomas in the choroid or in the brain, but coexisting nevi of the head is not a part of von Hippel's disease or, as it is now described, Lindau's disease. Unless other nevi can be found in this case, it would seem wiser to consider this a typical case of von Hippel's disease or, more scientifically, angiomatosis retinae.

BLOOD VESSEL NEOPLASMS (HEMANGIOBLASTOMAS) AND MALFORMATIONS (VENOUS AND ARTERIOVENOUS ANGIOMAS) OF THE BRAIN: OCULAR, ROENTGENOGRAPHIC, NEURAL AND VISCERAL FINDINGS. DR. SAMUEL BROCK and DR. CORNELIUS DYKE.

Following the work of Cushing and Bailey (Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C. Thomas, 1928), "tumors" of the blood vessels are divided into two large groups, true neoplasms—hemangioblastomas—and vascular malformations. Knowledge concerning the hemangioblastomas developed through studies made in cases of angiomatosis retinae. This disease first affects one eye and then usually the other. It starts in the early twenties or earlier, and

is apt to show strong familial tendencies. The gradual occurrence of secondary changes in the retina (reactive gliosis, subretinal exudate, cyst formation, retinal detachment and secondary glaucoma) obscures the primary pathology. Moreover, the original retinal picture may be further obscured by the advent of papilledema and postneuritic atrophy owing to the development of a cerebellar hemangioblastoma. Some authors have disputed the primary angiomatous nature of the process, believing that a gliomatous or endotheliomatous element is the predominating feature.

In 1926, Lindau showed that while angiomatosis retinae may occur alone, it is apt to be part of a much more widespread process. He described the central nervous lesions, the most important being involvement of the cerebellar hemisphere, in which one finds a small, well circumscribed, reddish-gray tumor, usually lying in the wall of a cyst which contains a yellow fluid. The cyst arises from plasma seeping into tissue spaces. In addition to a large cyst, there are often smaller cysts within the hemangioblastoma nodule. Occasionally, one encounters solid tumors. These hemangioblastomas also occur in the brain stem and spinal cord, and may be multiple. No instance of a cerebral hemangioblastoma is on record. Microscopic examination discloses capillary hyperplasia, proliferation of endothelial cells, small giant cells and cavernous spaces in the interstitium. The typical pseudoxanthomatous cell has a large cytoplasm containing lipoid or fatty granules and eccentric nuclei. Lindau believed that these are phagocytic endothelial cells picking up broken-down nerve elements. Cushing and Bailey pointed out that the interstitial reticular tissue one finds in these lesions is evidence of new growth in contradistinction to the interstitium of native brain tissue noted in the malformations. If associated with angiomatosis retinae, the symptoms of tumor usually begin to manifest themselves a number of years after the appearance of the retinal lesion.

Just as angiomatosis retinae may occur with no central nerve involvement, so cerebellar hemangioblastoma frequently occurs without any retinal angiomatosis. Of interest in this connection is a case reported by Vincent and Rappaport, that of a woman with a cerebellar hemangioblastoma whose son was afflicted with angiomatosis retinae.

This type of neoplasm constitutes about 1 per cent of tumors of the brain.

In the viscera multiple benign nonangiomatous cysts occur, especially in the pancreas, kidney, suprarenal gland, liver and epididymis. Hypernephroma and suprarenal adenoma may coexist.

According to Lindau, the malady is due to a disturbance in the development of the mesoderm in the third month of fetal life, with mesenchymal (vascular and gland) inclusions. The similarity of this disease to tuberous sclerosis and neurofibromatosis has been stressed. Yakovlev and Guthrie have described cases showing an overlap of the signs of these three syndromes.

The second large group, malformations of the cerebral blood vessels, comprises lesions composed of vessels lying in an interstitium of native brain tissue. Three varieties are distinguished: 1. Telangiectases are made up of capillary vessels. These are the so-called cavernomas, which are apt to occur in the upper pons and floor of the fourth ventricle. They may be multiple and have a familial incidence, but are of little

clinical interest. 2. Venous angiomas or varices are superficial lesions, which may, however, penetrate deeply into the brain substance. 3. Arteriovenous or arterial angiomas are also of a superficial and deep variety. A racemose collection of vessels or a single large artery with a small racemose lesion may be present. The deep-seated lesions are important. Dandy has made an important contribution to this subject. At operation arterial blood may be seen spurting into the veins; there is no capillary bed. Some believe that all arterial angiomas are venous angiomas which have undergone arterialization. Dandy pointed out that these malformations arise through defective development of the primordial vascular plexus. Indeed, a retention of the embryonic system of vessels is to be noted. Direct end-to-end communications between artery and vein as well as the angiomatous variety are found. These "growths" constitute another 1 per cent of tumors of the brain.

Eight cases of malformations of the cerebral blood vessels were presented. Two were venous lesions, five arteriovenous and one a venous lesion undergoing arterialization. In four, extracranial vascular lesions coexisted.

DISCUSSION

DR. ERNEST F. KRUG: Dr. Brock has given a complete record of this patient, whom I was fortunate enough to see with him. The fundus was seen at the last meeting of the New York Ophthalmological Society. It is a fortunate coincidence that Dr. McDannald was able to present his patient tonight with the identical fundus picture. Our patient died and we were able to get permission for an autopsy. I have here the eye, showing the great enlargement of the retinal veins. This picture (shown on the screen) depicts the congenital angiomatous lesion on the right side of the face. Here is the fundus (demonstrated), the disk entirely obscured by a mass of greatly enlarged and tortuous veins. At no place could I detect the communication between vein and artery. You have heard from Dr. Brock that this venous plexus extended back along the optic nerve, the chiasm, into the midbrain. There are few references in the literature to this particular type of aneurysmal malformation.

DR. RALPH I. LLOYD: Dr. Lloyd reviewed the history of angiomatosis retinae, citing the case reports by von Hippel (1899), Czermak (1891), Fuchs (1892), Wood (1892) and others.

DR. THOMAS K. DAVIS (by invitation): I shall not endeavor to discuss the hemangioblastomas, which are the typical true neoplasms, but shall rather speak of the angiomatous malformations which Dr. Brock has emphasized also, and recur to the thesis which he mentioned briefly, namely, the one recently presented by Guthrie and Yakovlev. This shows the relationship of the angiomatoses to two important syndromes, namely, von Recklinghausen's disease and tuberous sclerosis, all three being a neurocutaneous syndrome; i. e., in all three the chief sites of involvement are ectodermal structures; the nervous system, including the retina, and the skin. Dr. Brock has mentioned that the diseases appear in such varied forms that what is typical for neurofibromatosis may appear in a case labeled tuberous sclerosis, and even may appear in angiomatosis. The condition is traced back to the ectodermal tissues. When there is an angiomatous lesion on the face, it follows the sympathetic nervous system distribution, and that appears to indicate that the inaugurating situation is in the ectodermal tissue.

DR. JOHN WYCKOFF (by invitation): The symptoms that these patients have are those which any person has when veins and arteries anastomose directly and there are no interposing capillaries. The symptoms may be divided into two groups, those which occur at the instant when such an anastomosis takes place and those which are secondary. At the instant when such an anastomosis takes place, there is a fall in the systolic pressure, but the diastolic pressure falls much more, and there is not only a fall in the mean pressure, but an increased pulse pressure. With this venous overflow and low capillary circulation, the arterial and alveolar carbon dioxide is low. When these various things happen, in the first place there is a loss of vagal tone, and with it there is tachycardia. One of the first symptoms is a moderate tachycardia. Owing to the diminished carbon dioxide there are secondary changes in the heart muscle. The heart tends to enlarge, usually the mitral valve is affected and there is a systolic murmur at the apex. Owing to the increased pulse pressure one sees the typical changes of aortic insufficiency, and these cases are often thought to be cases of aortic insufficiency, if the patients are not carefully examined. There is an increase in the pulse pressure, a water-hammer pulse, capillary pulsation, and slow conduction of the pulse wave. As Dr. Brock said, the amount of blood that is shunted through one of these connections between arteries and veins is tremendous, and because of this, the blood vessels coming to the area and the veins going away from it become enormous; this being the point of least resistance in the circulation, more and more blood passes through, unless calcification takes place and further dilatation is stopped. When these communications become very large and the pulse pressure very low, secondary physical signs appear. These are much the same as the physical signs that occur with aortic insufficiency. A systolic thrill and a systolic murmur over the carotid are apt to develop. This happens because with the fall of diastolic pressure in the vessels they tend to collapse, and with the sudden flow of blood they are thrown into vibration, which gives rise to a thrill and a murmur. In addition, one must remember that whenever one congenital lesion is present, there may be other congenital lesions. I should not be surprised if one would meet in this type of case true congenital lesions of the heart as well as congenital lesions of the blood vessels.

DR. CLYDE E. MCDANNALD: I should like to record a case that fits in with these findings. This case has not been studied or worked out thoroughly yet. There is nothing particularly striking in the history. The patient is a woman, 24 years old, married, with two children. She has one brother who is insane, and her maternal grandmother and one or two maternal aunts were insane. She has brothers and sisters who are well. She remembers having some diseases of childhood, but does not seem to know which they were. I shall not attempt to describe these large tortuous veins. I am sure that the impression gained from seeing this case will be far more lasting than anything that I might say about it. Vision in that eye is reduced to perception of light. Vision in the other eye is normal. It is impossible for me to distinguish the veins and arteries in this case.

VENOUS ANGIOMA OF THE RETINA, OPTIC NERVE, CHIASM AND BRAIN: REPORT OF A CASE, WITH POSTMORTEM OBSERVATIONS. DR. ERNEST F. KRUG and DR. ERNEST P. KRUG.

This article will be published in full in a later issue of the ARCHIVES.

GERMAN OPHTHALMOLOGICAL SOCIETY

Forty-Ninth Meeting, Leipzig, May 19-21, 1932

ABRIDGED TRANSLATION BY PERCY FRIDENBERG, M.D., NEW YORK

(*Klin. Monatsbl. f. Augenh., June, 1932*)

(*Continued from page 156*)

II. Scientific Session, May 20

SYPHILITIC INFECTION AND CORNEAL REACTION TO FOREIGN SERUM. DR. VOM HOFE, Cologne.

Rabbits were tested for their reaction to a single intracorneal injection of from 0.05 to 0.1 cc. of inactive horse serum after the artificial production of a scrotal chancre. All reacted much more strongly than normal rabbits, whether the infection was of recent date or of long standing. The symptoms ranged from mild ciliary injection with exudation in the peripheral portions of the cornea to marked circumcorneal flush with signs of severe irritation in the cornea and iris. Histologic examination revealed interstitial keratitis with massive neoformation of vessels, copious exudate in the anterior chamber, and leukocytic infiltration of the iris, ciliary body and neighboring sclera. No spirochetes were found.

PATHOGENESIS OF ALBUMINURIC RETINITIS. DR. KYRIELEIS, Hamburg.

A girl, aged 11 years, had cystopyelonephritis, renal abscesses, contracted kidney and extensive bilateral detachment, with hemorrhages and contraction of the arteries. The most marked pathologic changes (cystic degeneration, fatty infiltration, etc.) were found in the internuclear layer. In the detached area the changes were much more marked from the equator, forward, in the choroid as well as in the retina, and the most marked lesions were located in the inner reticular layer. This would indicate that detachment interrupts the normal interplay of choroidal and retinal circulation so that the pathologic changes take place mainly in the terminal portions of the now independent vascular areas. The significance of the choroidal circulation in the pathogenesis of albuminuric retinitis seems to be at least as great as that of the retina.

EXPERIMENTAL REGENERATION OF THE RETINA. DR. BUECKLERS, Tuebingen.

The retina of one eye was removed in one hundred frog embryos. After partial extirpation there is a provisional closure of the wound by proliferated pigment epithelium. On this several layers of undifferentiated retinal cells (*Blastem*) form, arising from the adjacent parts. Both tissues proliferate into the vitreous. Differentiation of the *Blastem* into the typical layers begins at the base, and after this metamorphosis regeneration proceeds uninterruptedly. After total extirpation, regeneration

takes place from the posterior surface of the iris, probably from cells of the pars iridica retinae remaining attached. The vitreous framework is regenerated from the hyaloid membrane (membrana limitans interna). The more or less degenerated optic nerve is also restored gradually. Regeneration takes place in the absence of any connection with the central nervous system.

EXPERIMENTAL TREATMENT OF TETANY CATARACT. DR. IGERSHEIMER, Frankfort.

After removal of the parathyroids, the symptoms, especially the attacks of tetany, can be controlled by a special diet. The question was whether lens opacities were prevented or cleared or their progress checked by this treatment. Rats were put on Blum's blood diet, consisting of blood, milk and bread, with calcium lactate, and treated with injections of parathyroid extract-Collip. The controls were fed meat, which generally accentuated the tetanic attacks. In the first series, opacities of the lens came on decidedly later than in the others, and if the animals were changed to a "tetanophile" meat diet, progressed noticeably as they did in the controls on a meat diet if they were kept on that fodder after the appearance of changes in the lens. If the latter animals were put on an antitetanic diet, the opacities occasionally remained stationary or progressed more slowly and only slightly. Some even retrogressed, but this may have been spontaneous.

GENESIS OF HEAT CATARACT. DR. GOLDMANN, Bern, Zwitzerland.

Experiments on rabbits show that changes in the lens after long exposure to firelight are due to heat rays which produce posterior polar opacities when they fall on the iris alone but not when they are made to play for the same length of time on the lens alone. Thermo-elements could be made to heal into these eyes, in different places, without causing irritation. When the animals were brought into the work place of firemen, as great an increase of temperature (up to several degrees) was indicated behind the iris as was used to produce posterior polar opacities. Both long and short wavelengths were active. The outer temperature and that of blood act definitely on the temperature of the anterior lens surface behind the iris. The heating due to direct absorption of light rays by the lens alone is much too slight in the case of workers at forge fires, etc., to cause any changes in the lens.

EXPERIMENTS ON THE GENESIS OF CATARACT. DR. MUELLER, Basel, Switzerland.

The aqueous decolorizes methylene blue (methylthionine chloride, U.S.P.) and reduces oxygen. It was thought that this might be a factor in the metabolism of the lens. Electrometric methods and biochemical determination of the redux potential by means of indicators in the aqueous of cows and rabbits showed metabolism of an approximately reversible nature. The reducing power is markedly lowered soon after poisoning with naphthalin, and is still decidedly below normal in the aqueous refill. It is found in only a small amount in cows with cataract.

DISCUSSION

DR. MEESMANN, Berlin: In experiments with firelight cataract there were marked paralysis of the sphincter pupillae and depigmentation of the iris. In a larger series, excluding marked irritation of the iris, the results were absolutely negative, in spite of repeated irradiations for over 300 radiation hours, extending over two years. In firelight cataract in human beings there are no evident iridic changes, but the markedly delayed reaction to mydriatics has invariably attracted attention.

DR. FISCHER, Leipzig: The last researches of Vogt's school with albino rabbits showed a development of opacities without a period of latency. Heat may affect the oxygen exchange of the lens, which, as shown by the work of Comberg, Goldschmitt, Kronberg and others, has a very active metabolism.

DR. JESS, Giessen: Our attempts to induce cataract in white rats by destroying the parathyroid epithelial bodies met with difficulties in the form of spontaneous punctate, lenticular opacities, congenital or developing immediately after birth. Strangely enough, they may retrogress and clear up completely. This objection might be raised to the animal material used by Igersheim.

DR. COMBERG, Berlin: Dr. Comberg claims to have been the first (Heidelberg, 1930) to call attention to the quite uniform earliest appearance of opacities at the posterior pole as a result of the action of radiant energy from ultraviolet rays, roentgen rays and radium. This is an indication that in all these cases the underlying pathogenic factor, which is pretty much the same in all cases, must be a disturbance of the lens metabolism. The middle portion of the posterior capsule is only one-fourth as thick as the other portions, so that here, as well as in the sutural lines of the lens fibers, the two end-barriers, there must be the most active exchange with an increased demand on the metabolism of the lens.

DR. IGERSHEIMER, Frankfort: The rats were carefully examined with the slit-lamp for congenital opacities, and all were rejected which showed the slightest spontaneous changes. Dogs and cats also show cataractous changes after removal of the epithelial bodies, but were not used for systematic therapeutic experiments.

DR. GOLDMANN, Berlin: There is a small temperature interval or spread from severe changes in the iris to almost none when posterior polar opacities develop. In my experiments, there were no sphincter lesions, as the pupil and central portion of iris were shut off by a diaphragm. Of course, the root of the iris and the ciliary body were included in the irradiation. The factor of indirect metabolism via the ciliary body might be determined by the positive or negative effect on the development of opacities of a blackened bit of gold foil allowed to heal into the iris instead of excision of a portion of that structure in albino rabbits. Extremely intense irradiation will, of course, cause opacities of the lens just as it can be made to boil water. Vogt worked with low outer temperatures and cooled off the anterior surface of the lens. Such conditions are never present in work at open fires. The metabolism of the lens is highly sensitive to temperature and very active if reckoned on the basis of its surface, which alone is "living." Of

course, in proportion to the dry (dead) weight of the entire lens this portion is very small. Direct action of heat on the posterior pole can be excluded by the fact that opacities develop only in that portion of the lens star which corresponds to fibers which have been heated in front, under the iris. Undoubtedly, special conditions at the posterior pole favor the development of local opacities at that point. Experiments in which the irides are rendered artificially anemic are open to objection from the technical standpoint, because the temperature and the cooling conditions of the eye are then completely changed. The rise of temperature with diathermy generally lasts so short a time and is so slight that one need hardly fear any great damage to the eye unless one uses current intensities which are so extreme as to cause severe intraocular lesions otherwise.

Ocular Tuberculosis and Physique. Dr. Brueckner and Dr. A. Gigon, Basel, Switzerland.

Progressive phthisis and ocular tuberculosis are known to stand in a certain reciprocal antagonism, and uveal tuberculosis is much rarer in Nordic than in Alpine Germany, including in particular, Basel. The broad, undersized, "pyknic" build of southern Germans and Swiss is noticeable in patients with ocular tuberculosis, who also show a rather high ratio of weight to height. This type has a natural high resistance to tuberculosis of the lungs and seems to be disposed to the ocular variety. The opposite holds good with the asthenic, delicate, consumptive physique.

Autohemotherapy of Anterior Tuberculosis. Dr. Schieck, Wuerzburg.

Experiments were conducted based on the fact that experimental tuberculosis of the uveal tract runs a much milder course if the inoculations are made into the blood stream than if they are given via the anterior chamber. The protective quality of the blood might be made use of in tuberculosis of the iris by taking fresh blood from a vein in the patient's arm and injecting it into the anterior chamber after letting the aqueous flow off. Twenty-five patients were treated in this way, with excellent results. Within a few days the fatty precipitates and the nodules on the iris and in the filtration angle disappeared. Relapses can, of course, take place by renewed bacillemia, i. e., metastasis by way of the blood stream. This source can be dried up only by active tuberculin therapy in addition to the local treatment.

Local Action of Autohemo-Injections into the Anterior Chamber of Rabbits. Dr. W. Riehm, Wuerzburg.

Fresh venous blood from the animal's own ear vein or from the right ventricle of the same species was used. Undefibrinated blood caused a severe fibrinoplastic iritis with marked plus tension (glaucoma of the anterior chamber) which may be so extreme as to cause spontaneous rupture of the globe at the limbus. The action of defibrinated blood is somewhat milder and the rise in tension less marked. The longer the blood has stood after removal of the fibrin, the milder the inflammation, the slower the coagulation of the injected blood and the quicker its

resorption and disappearance from the anterior chamber. After from eight to eleven days blood can still be seen in the anterior chamber, but clinically it appears to have lost all power to set up an inflammation.

RECIPROCAL RELATION OF OCULAR TUBERCULOSIS AND INTRATHORACIC FINDINGS. DR. WERDENBERG, Davos.

The normal antagonism of slight intrathoracic roentgen findings and severe ocular tuberculosis was confirmed in 60 per cent of four hundred patients examined clinically. This antagonism is, however, often deceptive, as the intrathoracic source of disease is glandular, does not show up on the roentgenogram and reveals its true severity indirectly in the character of the ocular and somatic involvement (masked parallelism). The accompanying mild pulmonary changes (dissemination) are to be looked on as an expression of the neighboring glandular disease source and not as the original source itself. In severe tuberculosis of the lung, phthisis with cavities, pneumothorax, etc., the opposite condition of inverse antagonism, with mild ocular involvement, is noted. Thirty per cent of the cases, however, showed marked parallelism of the pathologicohistologic lesions in both organs, in the benign, productive form with miliary deposits as well as in malignant exudative tuberculosis of the hilar glands and uveal tract. The primary source of disease is generally the lymphatic system, and this should engage therapeutic attention and activity at the earliest possible moment.

DISCUSSION

DR. WEGNER, Freiburg: In Freiburg, ocular tuberculosis is extremely common and very severe, particularly in the form of retinal periphlebitis (Manz, Axenfeld), and 80 per cent of the patients with iridocyclitis are tuberculous. Climate, alone, does not explain this. Physique may well be an important factor. As to autohemotherapy in tuberculosis of the iris, I recently saw a woman with fresh tuberculosis of the iris in whom the anterior chamber had been tapped twenty times. So it is not the paracentesis but the injection of blood which is the essential factor.

DR. GILBERT, Hamburg: The more carefully one examines and appraises the constitutional symptoms in combined tuberculosis, the more often one finds that the antagonism between ocular and intrathoracic findings is largely a false one. The parallelism comes out more clearly if one takes into consideration not only the thoracic and abdominal cavities but the cranial cavity as well. Meningeal irritation is one factor which should not be overlooked. Massive hemorrhage into the anterior chamber is rather unusual in tuberculosis of the iris. I have in mind three cases with a very slow course, all in women in the thirties or forties, with spontaneous hemorrhages from the iris which almost completely filled the anterior chamber. In two of these very sluggish cases, resorption of the extravasated blood was promptly followed by marked and lasting improvement. Nodules were absorbed which had persisted for weeks and months.

DR. LINKZ, Budapest, Hungary: There seems to be a connection between myopia and the asthenic (cyclothymic) physique, as there is between hyperopia and the sthenic (schizothymic) build. Ocular tuber-

culosis favoring the sthenic type might accordingly have something to do with the factor of eye strain incidental to the use of the hypermetropic eye, producing a "weak spot."

DR. WECKERT, Goslar: Blood injected into the anterior chamber may act as a foreign protein or as a local irritant, as blood is used to stimulate formation of a firm callus in bone surgery. In the former case, the time intervals and any increase in dosage must be considered in view of a possible anaphylactic reaction.

DR. MEISNER, Greifswald: Special anatomic and mechanical factors in the "closed capsule" of the globe are hazards in the case of tuberculosis, and tissue changes and final reactions which in any other part of the body might be considered favorable result in serious loss of function, e. g., detachment from scar contractions, glaucoma and a small focus in the macular region.

DR. JESS, Giessen: Von Hippel used to say that during cataract extraction a hemorrhage massive enough to fill completely the anterior chamber was almost an actual guarantee against postoperative infection. I have seen marked improvement in a case of severe tuberculous iridocyclitis of both eyes after extensive hemorrhages into the anterior chamber following roentgen therapy, to which, at that time, the good result was attributed. I am now inclined to think that the effect was due to the bilateral hemorrhage into the anterior chamber.

DR. BLAICKNER, Salzburg: The severity of ocular tuberculosis varies greatly in different localities. Racial and constitutional peculiarities seem to be more important than the factor of climate, but so far there is no clue. Kretschmer's schema does not seem suitable, especially if persons of different ages are compared promiscuously. Cases of tuberculosis of the uvea in women at the climacteric show a large percentage of the pyknic type, but here hormonal factors alone are decisive. Young subjects in my practice did not seem to be predominantly pyknic.

DR. BRUECKNER, Basel, Switzerland: It is doubtful if any relation between refraction and body type exists.

DR. SCHIECK, Wuerzburg: There is no foreign protein action in the patient's own blood, and this can produce no anaphylaxis. The barrier between blood and aqueous plays a rôle. The autohemo-injections have, of course, no effect on synechiae and vitreous opacities.

HEADACHE, OCULAR DISEASE AND INFECTIONS WITH KOCH'S BACILLUS. DR. W. MEERHOFF and DR. A. MEERHOFF, Montevideo, Uruguay.

There can be no "local" diseases. Exaggerated interest in visceral pathology hampers the advance of medicine. Physiologic processes like teething, puberty, growth, menstruation and involution, which under normal conditions of health are quite painless, are still regarded as the cause of a variety of ailments. The same "organistic" spirit pervades the entire body of present-day endocrinology. A dyscrinism is taken as a cause instead of being correctly interpreted as a simultaneous pathologic reaction which, like the complicating symptoms in other organs, is occasioned by a single underlying factor. Neurasthenia, systemic infec-

tion, astigmatism, vagotonia and sympathicotonia are understood in the same way. In cases of headache ascribed to astigmatism, the previous history and, even more, the present condition show a host of apparently insignificant pathologic phenomena, among them the symptom complex of a mild hypo-adrenia. But one and all are caused by a single underlying factor, that of infection with Koch's bacillus, as proved by cure following tuberculin therapy in dozens of patients. The ocular trouble disappears without spectacles, and the patient need not be given correction down to a tenth of a diopter à la Gallois and Flandin (*Presse méd.* 39: 918 [June 20] 1931).

DISCUSSION

DR. BIELSCHOWSKY, Breslau: Headache, the main symptom in so-called asthenopia, cannot be explained by anomalies of refraction or motility (heterophoria). Otherwise one could not understand how in exceptional cases quite minimal degrees of hyperphoria (1 or 2 degrees) cause marked discomfort, while in the great majority of patients with decidedly higher degrees of motor anomaly there is no complaint. This individually varying resistance must depend on a similarly varying individual disposition, especially of the nervous system, which, of course, may be acquired. Occupation, mode of life and other factors play a part. This by no means implies that while carefully considering the general condition and regimen one should neglect to correct accurately any ametrophia or heterophoria.

DR. BAHR, Oehynhausen: The cases of heterophoria just mentioned are not unusual. A "labile" nervous system is, of course, a complicating factor in headache and other asthenopic symptoms due to very slight degrees of ametropia or heterophoria. But these gradations occur everywhere and are not merely the products of an American population. They are equally common in the nervous inhabitants of large cities, in soldiers during a campaign and in a purely bucolic, absolutely "non-nervous" agricultural population. Besides, the headaches are almost invariably accompanied by gastric disturbances, particularly those of a spastic nature, dizziness and disturbances of the vegetative nervous system. The ocular muscles should be tested in every ocular examination. Slight vertical phorias are often overlooked, are not easily detected and may be concealed by spasm of the antagonists.

DR. W. MEERHOFF: The history of asthenopic patients frequently shows, besides headache, psychasthenia and neurasthenia, low blood pressure, nervous disturbances of digestion and gastric function and menstrual disturbances in women.

DEVELOPMENT OF IRIS MUSCULATURE. DR. R. SONDERMANN, Berlin.

This system arises from the mesoderm, not from the ectoderm. Besides undifferentiated mesenchymal cells the same obliterated primitive capillaries are concerned which play an important part in the development of Bruecke's ciliary muscle and in the uveal and uveoscleral trabecula. The development of the sphincter varies as the obliterated capillaries enter into a loose or, on the other hand, a close intercommunication with the pigment epithelium, particularly at the pupillary margin. In the first case, the rudiment or primordial anlage of the sphincter

shows a definitely vascular character. In the second, the pigment at the pupillary margin forms the sphincter and is organically to be considered as part of the iris, *sensu strictiori*. The pigment proliferations protruding from the basal cells of the pigment epithelium have the double purpose of binding the epithelium closely to the muscle and of walling off the muscle from the rest of the iris. The dilator develops from collections of connective tissue fibrils of the iris, which at the seventh month is in a state of active growth, and not, as generally believed, from protoplasma fibrils of the pigment epithelium.

Topography of the Ora Serrata. Dr. Stein, Prague, Czechoslovakia.

Systematic and careful measurements of histologic sections, as well as whole freshly enucleated eyes of various refraction categories and axial dimensions, show that within certain limits the distance of the ora from the corneal limbus, the breadth of the ciliary body, depends on the axial length of the globe. The shortest distance in sixty eyes was 4.8 mm. on the temporal, and 4.4 mm. on the nasal, side of the globe, with 6 diopters of hypermetropia in an eye 21 mm. long; the longest distance, 10.8 mm. on the temporal side in an eye with myopia of over 20 diopters and a 31 mm. axis. In axial hypermetropia as well as in axial myopia the anterior portion remains behind in relation to the entire size of the globe, and the distance of the ora serrata to the limbus is disproportionately short, the pars optica of the retina being lengthened at the expense of the pars ciliaris. The shorter the eye, the more marked is this disproportion. The orae are generally 8 mm. nearer the limbus on the nasal side. When they are equidistant, it is found that the insertions of the internal and external rectus muscles are too. There are a few anomalous forms due to developmental defect, with a histologic picture of invasion of the orbiculus by atypical islands of retinal tissue, proliferation of ciliary epithelium, reduplication of nuclei and other indications of a disproportionate development of the pars optica of the retina at the expense of the pars cocca.

Biology of Corneal Tissue. Dr. Loewenstein, Prague, Czechoslovakia.

A lipoid arcus can be produced in rabbits after adding small amounts of cholesterol oil to their feed. A bilateral juvenile lipoid arcus was noted in a boy of 12 years, who had had large doses of cod liver oil since early infancy. Alkali feeding (8 per cent sodium bicarbonate solution) caused a marked regeneration of corneal epithelium, and a 6 per cent solution injected conjunctivally seemed to increase resistance to staphylococcus infection, while acid feeding slightly decreased it and cholesterol feeding almost entirely destroyed it. The mild acidosis of wounds and inflammation is favorable to regeneration and resistance. Excessive degrees might be kept in check by feeding with alkali.

Catgut Anaphylaxis. Dr. Marchesani, Munich, and Dr. Knorr.

The intravenous injection into guinea-pigs of catgut extract or sheep serum, each of which sensitizes an organism for the other, caused ana-

phylactic symptoms and in some cases death. After similar preparation, the introduction of catgut sutures under the skin or into the anterior chamber was followed by an unusually intense local reaction with dense cellular infiltration, edema and hemorrhages, and in later stages with a delayed organization of connective tissue.

III. Scientific Session, May 20

DR. CLAUSEN, HALLE, *Presiding*

SUSCEPTIBILITY OF OPTIC NERVE TO STIMULATION BY ELECTRICITY. DR. BEST, Dresden.

Sensations of light on direct stimulation of the fibers of the optic nerve by galvanic irritation and electrical processes of various frequencies in the nerve have been considered by some as essential factors in the conduction of visual impulses and not merely concomitant phenomena. There is no proof of the possibility of an inadequate stimulus for the optic nerve. Mechanical irritation by pressure, as has long been known, causes no sensation of light. The electric reaction was tested in a case of malignant nasal neoplasm necessitating the removal of a seeing eye under local anesthesia. Ascending and descending galvanic currents, up to 4 ma., applied to the central nerve stump, failed to elicit any subjective sensations of light. One must therefore infer that the vital or metabolic processes in the conduction of visual stimulation are specifically different from those in sensory or motor nerves.

SENSIBILITY OF THE CORNEA. DR. FRANCESCHETTI, Basel, Switzerland, with DR. MUELLER and DR. PFLIMLIN.

Does corneal tissue have sensation only for pain or also for cold (only at the periphery [Frey]) and for pressure? Experiments with the return of sensation after the application of local anesthetics and analysis of the curves showed marked discrepancies after various concentrations, and the complicated formulas which had been calculated were found not to agree with the practical results. Best's research with 1 per cent butyn speaks in favor of a duality of sensations in the cornea.

RESEARCH WITH THE SPHERICAL ADAPTOMETER. DR. HERTEL, Leipzig.

Hertel uses a smaller simplified apparatus, but the principle of measurement remains the same. If the degree of illumination of the sphere wall is known, that of the pupil and, hence, of the retina, is also given. Several curves showed the importance of previous adaptation and the necessity of a point of fixation (red light point) in testing adaptation of various retinal points. It was found that there is a definite, constant increment in the intensity of lights which can just be distinguished from adapting lights of increasing density, in perfect accord with the basic formula of Weber-Fechner. The spherical adaptometer enables one to determine whether a person has sufficient ability to distinguish certain intensities of light, at work, in traffic or on special occasions, as in accidents.

DISCUSSION

DR. VOM HOFE, Cologne, and DR. FISCHER, Leipzig: Drs. vom Hofe and Fischer confirmed Best's observations in the chronaximetric studies. They could not elicit any subjective sensations of light in the optic nerve after enucleation. As phosphenes are not localized, one cannot relate them to the retina.

DR. ELSCHNIG, Prague, Czechoslovakia: If, after a perfectly painless cataract operation one applies tincture of iodine to the wound margins there is at once intense pain. Does this indicate a duality of sensation (Franceschetti)?

DR. ENGELKING, Cologne: Hertel's apparatus is admirable for scientific study but too costly and complicated for general practical use. Simpler methods are quite satisfactory. Preliminary adaptation with a bright surface is essential for every definite study of this function. If preadaptation is prolonged for more than forty-five minutes it is practically immaterial with what degree of light one started, as the curves of adaptation tend to coincide almost completely, and show for each person the same curve of function no matter what the starting point of light adaptation is. The fact that starting with various degrees of light adaptation Hertel's curves did not coincide indicates merely that preadaptation was not sufficiently long (twenty-five minutes) and that, as one might say, the first section of the curve was missing. Extreme, "eccentric" degrees of testing should be noted, as the sensibility of the rod apparatus shows marked variations under these conditions. The degrees of illumination in Hertel's studies were well within the zone of retinal functioning in which day apparatus and twilight apparatus are simultaneously active. The figures for the two sets can be combined in curves after using blue or mixed (white) light and twilight-free red light, respectively.

DR. MUELLER, Basel, Switzerland: Matthey has studied dark adaptation in fifty-four normal subjects of different ages and plotted a standard curve which is very useful in determining a pathologic alteration of the light sense. There seem to be four types of dark-adaptation, each with a special relation to the two terminal retinal apparatus.

(*To be concluded*)

Book Reviews

Biomicroscopic du corps vitré. By F. Koby. Price, 120 francs. Pp. 120, with 15 figures and 20 plates. Paris: Masson & Cie, 1932.

This is the latest of the excellent monographs on biomicroscopy sponsored by the French Ophthalmologic Society. The author first takes up the examination of the normal vitreous, and then deals in order with the posterior capsule, vitreous opacities in general, myopia, senescence and traumatic lesions of the vitreous. The final section is of exceptional interest and deals with alterations in the vitreous associated with various forms of ocular pathologic changes, notably intraocular inflammations and neoplasms, glaucoma and detachment of the retina.

The bibliography is carefully selected. The drawings, while necessarily somewhat diagrammatic, are beautifully done.

G. M. Bruce.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Prof. F. de Lapersonne, 217, Faubourg St. Honoré, Paris.
Secretary-General pro tem.: Dr. A. Churchill, 66, Boulevard St. Michel, Paris.

International Ophthalmologic Congress

Secretary: Dr. Francisco Poyales, Olozaga 3, Madrid.
Place: Madrid. Time: April 16-22, 1933.

FOREIGN

British Medical Association, Section on Ophthalmology

President: Sir J. Herbert Parsons, 54 Queen Anne St., Cavendish Square, London, W. I.

Ophthalmological Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgoam Road, Bombay 4.
Secretary: Dr. C. R. Athawale, Bhatwadi Girgoam, Bombay 4.
Place: A. M. C. Free Ophthalmic Hospital Bldg., Poi Bawadi Parel, Bombay 12.
Time: First Friday of every month.

Ophthalmological Society of the United Kingdom

President: Mr. A. H. H. Sinclair, 6 Charlotte Square, Edinburgh.
Secretary: Mr. Humphrey Neame, 56 Portland Place, London, W. I.
Place: London. Time: May 11-13, 1933.

Oxford Ophthalmological Congress

Master: Dr. Cyril Walker, Bristol, England.
Secretary: Dr. C. G. Russ Wood, Hill House, Abberbury Rd., Iffley, Oxford, England.

Royal Society of Medicine, Section of Ophthalmology

President: Dr. A. C. Hudson, 50, Queen Anne St., W. 1, London.
Secretary: Dr. J. D. Magor Cardell, 27, Weymouth St., W. 1, London.
Place: London. Time: June 9, 1933.

Société Française d'Ophthalmologie

Secretary: Dr. René Onfray, 6 avenue de la Motte Picquet, Paris 7è.

German Ophthalmological Society

Secretary: Prof. A. Wagenmann, Heidelberg.

NATIONAL

American Medical Association, Section on Ophthalmology

Chairman: Dr. Frederick H. Verhoeff, 82 Commonwealth Ave., Boston.
Secretary: Dr. Parker Heath, 1551 Woodward Ave., Detroit.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Ophthalmology and Oto-Laryngology

President: Dr. B. R. Shurley, 62 W. Adams Ave., Detroit.
President-Elect: Dr. J. M. Wheeler, 30 W. 59th St., New York.
Executive Secretary-Treasurer: Dr. William P. Wherry, 1500 Medical Arts Bldg., Omaha.
Place: Boston. Time: 1933.

American Ophthalmological Society

President: Dr. Thomas B. Holloway, 1819 Chestnut St., Philadelphia.
Secretary-Treasurer: Dr. J. Milton Griscom, 2213 Walnut St., Philadelphia.
Place: Washington, D. C. Time: May 8-10, 1933.

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* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

SECTIONAL

New England Ophthalmological Society

President: Dr. David W. Wells, Hotel Westminster, Boston.
Secretary-Treasurer: Dr. Theodore L. Terry, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

Pacific Coast Oto-Ophthalmological Society

President: Dr. Hans Barkan, 490 Post St., San Francisco.
Secretary-Treasurer: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Place: San Francisco. Time: June 28-30, 1933.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. John H. Harter, 1215 Fourth Ave., Seattle.
Secretary-Treasurer: Dr. Francis A. Brugman, 806 Cobb Bldg., Seattle.
Time: 8 p. m., third Tuesday of each month, except July and August.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. R. B. Smith, Alma, Mich.
Secretary-Treasurer: Dr. W. K. Slack, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw, Mich., or Bay City, Mich. Time: First Friday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. John B. Gregg, 101 S. Main St., Sioux Falls, S. Dakota.
Secretary-Treasurer: Dr. F. H. Roost, 420 Trimble Bldg., Sioux City, Iowa.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. William D. Gill, 323 Medical Arts Bldg., San Antonio, Texas.
Secretary: Dr. William A. Wagner, 914 American Bank Bldg., New Orleans.
Place: Richmond, Va. Time: November, 1933.

Southwestern Michigan Triological Society

President: Dr. W. E. McGarvey, 802 Jackson City Bank Bldg., Jackson.
Secretary: Dr. Don C. Lyons, 1405 Union and Peoples National Bank Bldg., Jackson.
Time: Third Thursday of alternate months.

STATE

Colorado Ophthalmological Society

President: A presiding officer is selected for each meeting alternately until all members have served.
Secretary: Dr. Ralph W. Danielson, 258 Metropolitan Bldg., Denver.
Place: Capitol Life Building, Denver. Time: 7:30 p. m., third Saturday of the month, October to April, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. J. J. Cohane, 59 College St., New Haven.
Secretary-Treasurer: Dr. Walter L. Hogan, 750 Main St., Hartford.
Time: May, November.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Thomas H. Hall, Jr., 617 Mulberry St., Macon.
Secretary-Treasurer: Dr. J. A. Smith, 700 Spring St., Macon.

Indiana Academy of Ophthalmology and Oto-Laryngology

President: Dr. Robert J. Masters, 805 Hume-Mansur Bldg., Indianapolis.
Secretary: Dr. J. Kent Leasure, 23 E. Ohio St., Indianapolis.
Place: Indianapolis. Time: December 13, 1933.

IOWA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY
President: Dr. W. W. Pearson, 410 Sixth Ave., Des Moines.
Secretary-Treasurer: Dr. W. F. Boiler, 105 E. Iowa Ave., Iowa City.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
Chairman: Dr. Wilfred Haughey, 303 Post Bldg., Battle Creek.
Secretary: Dr. H. O. Westervelt, 239 Pipestone St., Benton Harbor.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY
President: Dr. Harold J. Rothschild, 239 Lowry Bldg., St. Paul.
Secretary-Treasurer: Dr. Walter E. Camp, Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY
President: Dr. Lawrence G. Dunlap, 101 Main St., Anaconda.
Secretary: Dr. A. W. Morse, Phoenix Bldg., Butte.
Place: Anaconda. Time: July 11, 1933 (meetings are held semi-annually).

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY
Chairman: Dr. Charles H. Schlichter, 556 N. Broad St., Elizabeth.
Secretary: Dr. B. E. Failing, 31 Lincoln Park, Newark.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION
Chairman: Dr. D. F. Gillette, 109 S. Warren St., Syracuse.
Secretary: Dr. Frank M. Sulzman, 1831 Fifth Ave., Troy.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY
President: Dr. Axel Oftedal, 55½ Broadway, Fargo.
Secretary-Treasurer: Dr. F. L. Wicks, 516 Fourth St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY
President: Dr. A. B. Dykman, Medical Dental Bldg., Portland.
Secretary-Treasurer: Dr. Andrew J. Browning, 418 Mayer Bldg., Portland.
Place: Good Samaritan Hospital. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY
President: Dr. Herman A. Winkler, 224 Thayer St., Providence.
Secretary: Dr. N. A. Bolotow, 108 Waterman St., Providence.
Place: Rhode Island Medical Library. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. J. W. Jervey, Jr., 101 Church St., Greenville.
Secretary: Dr. Walter Bristow, Medical Bldg., Columbia.
Place: Columbia. Time: October, 1933.

TENNESSEE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY
President: Dr. R. G. Reaves, 422 W. Cumberland Ave., Knoxville.
Secretary-Treasurer: Dr. Ralph O. Rychener, 1720 Exchange Bldg., Memphis.
Place: Nashville. Time: April 10, 1933.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY
President: Dr. W. D. Jones, 3116 Live Oak St., Dallas, Texas.
Secretary: Dr. A. F. Clark, 1034 Nix Professional Bldg., San Antonio.

UTAH OPHTHALMOLOGICAL SOCIETY
President: Dr. D. W. Henderson, 75 S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. T. F. Welch, 14 Exchange Pl., Salt Lake City.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY
President: Dr. Frank P. Swart, 142 W. York St., Norfolk.
Secretary-Treasurer: Dr. H. G. Preston, 307 Professional Bldg., Harrisonburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. O. H. Bobbitt, Medical Arts Bldg., Charleston.
Secretary: Dr. Harry V. Thomas, 95 Fairmont Ave., Fairmont.

LOCAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Elbert A. Curtis, 65 Central St., Newark.
Secretary: Dr. A. Russell Sherman, 671 Broad St., Newark.
Place: 91 Lincoln Park South. Time: 8:45 p. m., second Monday of each month.

ACADEMY OF MEDICINE OF TORONTO, SECTION OF OPHTHALMOLOGY

Chairman: Dr. P. J. F. Houston, 34 Hurndale Ave., Toronto.
Secretary: Dr. Alexander E. MacDonald, 151 Bloor St., W., Toronto.
Time: First Monday of winter months.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. L. C. Rouglin, 127 Peachtree St., N. E., Atlanta, Ga.
Secretary: Dr. William O. Martin, Jr., Medical Arts Bldg., Atlanta, Ga.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: 8 p. m., last Thursday of each month.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Harry Friedenwald, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. William M. Rowland, 906 Cathedral St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. W. F. C. Steinbugler, 515 Ocean Ave., Brooklyn.
Secretary: Dr. Walter V. Moore, 1 Nevins St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. H. D. Andrews, 33 Allen St., Buffalo.
Secretary-Treasurer: Dr. Thurber Le-Win, 112 Linwood Ave., Buffalo.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Michael Goldenburg, 104 S. Michigan Ave., Chicago.
Secretary: Dr. Richard C. Gamble, 30 N. Michigan Ave., Chicago.
Place: Medical and Dental Arts Club. Time: Third Monday of each month from October to May.

CLEVELAND ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

Chairman: DR. M. W. Jacoby, 2323 Prospect Ave., Cleveland.
Secretary: Dr. H. C. Rosenberger, 1065 Rose Bldg., Cleveland.
Place: Winton Hotel. Time: Fourth Friday of each month.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Roy B. Metz, Hanna Bldg., Cleveland.
Secretary: Dr. Paul G. Moore, Medical Arts Bldg., Cleveland.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. L. F. Appleman, 308 S. Sixteenth St., Philadelphia.
Clerk: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. John B. Alcorn, 167 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Edward W. Harris, 681 E. Broad St., Columbus, Ohio.
Time: First Monday of each month.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. O. M. Marchman, 1717 Pacific Ave., Dallas, Texas.
Recording Secretary: Dr. W. Mood Knowles, 1717 Pacific Ave., Dallas, Texas.
Corresponding Secretary: Dr. J. M. Potts, 1717 Pacific Ave., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. Cecil C. Jones, 1121 Equitable Bldg., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month, September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Raymond S. Goux, David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. R. H. Seeley, 9 Court St., Rutland, Vt.
Secretary-Treasurer: Dr. Arthur F. Holding, 142 Washington Ave., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. H. Needham, 1304 Medical Arts Bldg., Fort Worth, Texas.
Secretary-Treasurer: Dr. Van D. Rathgeber, 1011 Medical Arts Bldg., Fort Worth.
Place: University Club. Time: 6:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Carl F. Snapp, 26 Sheldon Ave., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Walter W. Oliver, 26 Sheldon Ave., Grand Rapids. Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. J. F. Gamble, 201 Main St., Houston, Texas.
Secretary: Dr. B. F. Payne, 1304 Walker Ave., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-Laryngological Society

President: Dr. John W. Carmack, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Albert N. Lemoine, 906 Grand Ave. ,Kansas City, Mo.
Secretary: Dr. Harold B. Hedrick, 618 Professional Bldg., Kansas City, Mo.
Time: Third Thursday of each month from September to May. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

President: Dr. Ferris L. Arnold, 923 Security Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. Clyde E. Harner, 312 Security Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from September to June.

Los Angeles County Medical Society, Section on Ophthalmology and Oto-Laryngology

Acting President: Dr. D. E. Godwin, 910 Security Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. F. H. Brandt, 1052 W. Sixth St., Los Angeles.
Place: Elks Temple. Time: 6:30 p. m., fourth Monday of each month from September to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Oto-Laryngology

Chairman: Dr. Albert P. Tibbets, 1801 I St., Washington.
Secretary Dr. G. Victor Simpson, Rhode Island Ave., Washington.
Place: 1718 M St., N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Oto-Laryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. R. O. Rychener, Exchange Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month. Annual meeting, Jan. 10, 1933.

Milwaukee Oto-Ophthalmic Society

President: Dr. T. F. McCormick, 324 Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. O. P. Schoofs, 324 E. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., third Tuesday of each month.

Montreal Ophthalmological Society

President: Dr. J. P. E. Bousquet, 66 Sherbrooke St., West, Montreal, Canada.
Secretary: Dr. J. A. MacMillan, 1410 Stanley St., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Hilliard Wood, 700 Church St., Nashville, Tenn.
Secretary-Treasurer: Dr. H. C. Smith, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. Charles A. Bahn, 150 Baronne St., New Orleans.
Secretary-Treasurer: Dr. M. F. Meyer, Canal Bank Bldg., New Orleans.
Place: Eye, Ear, Nose and Throat Hospital. Time: Third Thursday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Mark J. Schoenberg, 1160 Park Ave., New York.
Secretary: Dr. Algernon B. Reese, 73 E. Seventy-First St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. L. G. Howard, 532 First Ave., Council Bluffs, Iowa.
Secretary-Treasurer: Dr. W. A. Cassidy, 1620 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Edward B. Heckel, Jenkins Arcade Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Pittsburgh Slit-Lamp Society

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: 121 University Pl. Time: Second Monday evening of every month, except June, July and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. William R. Weisiger, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. R. W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

Chairman: Dr. E. S. Amsler, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. E. W. O'Brien, 5 N. Goodman St., Rochester, N. Y.
Place: Rochester Medical Association, 113 Prince St. Time: 8 p. m., third Monday of each month from October to May.

St. Louis Ophthalmic Society

President: Dr. Julius H. Gross, Carleton Bldg., St. Louis.
Secretary: Dr. Carl T. Eber, 1006 Carleton Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Charles J. Boehs, Medical Arts Bldg., San Antonio, Texas.
Secretary-Treasurer: Dr. E. D. Dumas, 425 Medical Arts Bldg., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Robert C. Martin, 384 Post St., San Francisco.
Secretary: Dr. George N. Hosford, 490 Post St., San Francisco.
Place: Society's Building, 2180 Washington St., San Francisco.
Time: Third Tuesday of every month except May, June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. J. L. Scales, Medical Arts Bldg., Shreveport, La.
Secretary-Treasurer: Dr. W. L. Atkins, 505 Medical Bldg., Shreveport, La.
Place: 1240 Texas Ave. Time: 7:30 p. m., first Monday of each month from October to June.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. David Hartin, Old National Bank Bldg., Spokane, Wash.
Secretary: Dr. W. W. Henderson, Paulsen Medical and Dental Bldg., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. W. G. Dickinson, 504 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. Harold H. Joy, 504 State Tower Bldg., Syracuse, N. Y. N. Y.
Place: University Club. Time: Second Friday of each month except June, July and August.

Tulsa Academy of Ophthalmology and Otolaryngology

President: Dr. Roy Dunlap, 108 W. Sixth St., Tulsa, Okla.
Secretary-Treasurer: Dr. Marvin D. Henley, 108 W. Sixth St., Tulsa, Okla.
Place: Medical Arts Bldg. Time: Monthly.